The New England
Journal of Medicine

Copyright, 1949, by the Massachusetts Medical Society

Volume 241 SEPTEMBER 1, 1949 Number 9

MEDICAL CONSIDERATIONS IN THE CARE OF ELDERLY PATIENTS WITH HIP FRACTURES*

ROBERT J. FAHEY, M.D.,† RICHARD M. KILFOYLE, M.D.,‡ AND JOSEPH H. SHORTELL, M.D.§

BOSTON

IN SHARP contrast to the attitude of a few years back, hip nailing in aged people suffering from various medical disabilities has become accepted surgical practice. Penicillin, carefully controlled anesthesia, the use of blood and standard physiologic fluids, refinements of surgical technic and early ambulation have permitted feats of major surgery previously believed impossible, especially in the aged. In the cases of hip fracture, traction or a plaster spica was used by choice under the impression that operation was too great a risk in this age group. This attitude is now reversed, and nailing is performed to avoid the many evils of prolonged bed rest and traction, to diminish the burdens on an already overtaxed nursing staff and, most important, to lower an appalling mortality rate.

The serene course of some patients with even critical medical conditions both during and after operation has been surprising. With good medical care and follow-up study and careful selection of patients and time of operation, a satisfactory outcome is now expected. Nevertheless, some deaths have occurred postoperatively in patients who were judged acceptable for hip nailing — usually from conditions that were present before the operation or even the fracture. The most important medical factors, therefore, have not been emphasized in the literature on hip fracture. No criteria have been established regarding selection of the patient and the time of operation or what definite measures can be taken under specific circumstances to facilitate surgery or make it possible.

To clarify our thoughts in the matter with the purpose of holding operative mortality to a minimum, we studied the records of 100 consecutive patients who had attained the age of seventy or over, who were treated on the Sixth Surgical Service, Boston City Hospital, for fracture of the hip. The periods of treatment were between November, 1944, and January, 1948. This was a period in which penicillin was in general use — a factor that, we believe, had an important bearing on the general clinical course. No attempt was made to include follow-up studies inasmuch as this paper deals with the medical care in the hospital until the patient is ready for discharge.

In this series, the operation of nailing was done by one of two methods: "open" in the operating room or by the so-called "closed" method under the fluoroscope. The first was more frequently used.

The patient was given light premedication and was transported to the operating room with the injured limb supported on a Thomas splint. Low spinal anesthesia of light dosage was given, and intravenous injection of saline solution was started and allowed to run slowly.[1] Two pints of blood were ready if needed. The fracture was reduced by a suitable method, a modified Leadbetter maneuver or, in the cases of some intertrochanteric fractures, traction with internal or external rotation. X-ray films taken with a portable apparatus were used to check the position. After skin preparation and draping, the upper femoral shaft was approached through a straight or curved lateral incision, deepened through fascia lata and vastus lateralis. Sufficient periosteum was elevated to permit insertion of two Bennett retractors. Fixation depended on the type of fracture and the judgment of the operator. Kirschner wires and x-ray films taken with a portable apparatus were used to find proper length and direction.

The "closed" method was performed in the dark room with the aid of the fluoroscope. Reduction may be checked by a film taken with the casette placed in the viewing screen. Kirschner wires were then drilled across the fracture site through the prepared skin. An incision, 2.5 cm. in length, was made down to bone around the correctly placed wire. A cannulated Smith-Petersen nail was threaded over the wire and driven home. This procedure

*Presented in part at the annual meeting of the American College of Surgeons, Committee on Fractures and Other Traumas, Boston, January 29, 1949, and at the Boston City Hospital postgraduate course in fractures, conducted by Sir Reginald Watson-Jones, May, 1948.

From the Sixth Surgical and the Third Medical Services, Boston City Hospital.

†Instructor in medicine, Tufts College Medical School; formerly, resident, Third Medical Service (Tufts), Boston City Hospital.

‡Assistant resident, Children's Hospital, Children's Medical Center; formerly, resident, Sixth Surgical Service, Boston City Hospital.

§Instructor in orthopedic surgery, Harvard Medical School; surgeon-in-chief, Boston City Hospital; chief, Sixth Surgical Service, Boston City Hospital.

could be completed very often in thirty or forty minutes, which, together with the minimal operative trauma, constituted its chief advantage.

Postoperative care was aimed to get the patient either out of bed or moving about freely in bed as soon as possible, and as soon as strength and freedom from pain allowed. Sometimes a day or two after operation a woman in her middle eighties was up in a chair, surprised and smiling at how well she felt. Quadriceps exercises and knee motion were encouraged; daily check was made for common complications, especially calf tenderness, pain and foot edema. Again, when strength was sufficient, usually a matter of two or three weeks, the patient was allowed up in a walker and then on crutches under supervision. The foot on the injured side was placed on the floor, with very little or no weight bearing, to avoid the awkwardness of crutch walking with the hip and knee flexed.

Time of discharge depended on many factors, most of them social.

Seventy-two of the 100 patients were operated upon. Twenty-eight were treated conservatively either by traction or by application of a plaster spica. Conservative treatment was instituted because of personal choice of the attending surgeon, because of the nature of the fracture or because the patient was considered a poor surgical risk. Sixty-one had intertrochanteric fractures, and 39 fractures of the femoral neck. Of the patients operated upon, 13 died—a mortality of 18 per cent. In the group treated conservatively there were 9 deaths—a mortality of 32 per cent. The high mortality in this group reflects the fact that it included many poor-risk patients. The average time in the hospital prior to surgery was nine and four-tenths days. The patients operated on were out of bed, on the average, in twelve and five-tenths days, and those treated conservatively in forty-one days. The average hospital stay was forty-five days for the operated patients and seventy-seven days for those treated conservatively. These statistics differ little from reports of several other large clinics.[3-8]

TABLE 1. *Medical Grouping of All Patients.*

GROUP	STATUS OF PATIENT	SURVIVALS	DEATHS	TOTALS
I	No detectable disease process ...	13	0	13
II	Mild to moderate reversible conditions	64	6	70
III	Severe, nonreversible conditions becoming worse	0	17	17

No attempt has been made to correlate the type of fracture with the mortality.

We have found that our cases could be classified into three groups (Table 1), depending upon the amount and type of concomitant medical disability existing as observed during their first few hospital days. In the first group were good operative risks, in the second fair operative risks and in the third patients on whom operation was contraindicated.

Group I

In Group I we placed patients who, in spite of their age, were in good physical condition. They tolerated surgery very well and required only the usual preoperative and postoperative care. Unfortunately, this was a small group. In our series of 100 cases, 13 fell into this category. There was no mortality. The following case is typical:

E. Q., a 76-year-old woman, entered the hospital on December 5, 1946, with a history of having slipped and fallen on her porch on the day prior to entry. After this accident she noted pain in the left hip and inability to stand. Physical examination showed shortening and external rotation, with painful motion of the left hip. The lungs were clear, the heart was not enlarged, and the rate and rhythm regular, with a soft apical systolic murmur. The blood pressure was 140/70. Routine laboratory work was negative. X-ray study showed an intertrochanteric fracture of the left hip. The patient remained in excellent physical condition in Russell traction. On the 5th day a Smith-Petersen nail with a Thornton attachment was inserted uneventfully. Anatomic reduction was obtained. The postoperative course was uneventful, and the patient was discharged on the 17th hospital day, on crutches, to be followed at home by her own doctor.

Group II

Group II included patients who showed the scars of aging. They had underlying physical disabilities that required active and prompt medical treatment prior to operation, cautious anesthetic and operative handling and a close postoperative follow-up study. That hip fracture in the elderly is very often as much a medical as a surgical problem can be seen from the fact that 70 cases fell into this group.

Four patients in this group died. A typical case is as follows:

S. M., an 83-year-old woman, entered the hospital on April 12, 1947, with a complaint of pain in the right hip after a fall on the night prior to admission. She also gave a history of long-standing diabetes and hypertension. The diabetes had been treated with diet alone, but she had been taking digitalis intermittently for the past year. Physical examination revealed a well developed woman in no apparent distress. The lungs showed moist rales at both bases. The heart border was enlarged to the anterior axillary line, and there was a rough, Grade III systolic murmur. The blood pressure was 190/100. There was shortening and external rotation of the right leg. The urine showed an orange Benedict reduction, and the sediment was loaded with white blood cells. Examination of the blood disclosed a hemoglobin of 65 per cent and a white-cell count of 8600. The blood sugar was 250 mg., and the nonprotein nitrogen 42 mg. per 100 cc., and the carbon dioxide combining power 49 per cent. X-ray examination showed an intertrochanteric fracture of the right femur. The right leg was placed in Russell traction, and immediate attempts to restore cardiac compensation and regulate the diabetes were instituted. The patient was given penicillin and sulfadiazine to combat the urinary-tract infection. By the 16th hospital day the diabetes was under good control, all evidence of cardiac decompensation had cleared, and the urine sediment was normal. She was then operated upon under spinal anesthesia. Smith-Petersen nail with a Thornton plate was successfully inserted. The postoperative course was smooth, and she was out of bed on the 4th postoperative day and discharged from the hospital on the 58th hospital day on crutches.

Group III

Group III comprised patients with severe and extensive medical problems who, under adequate medical management, showed no evidence of improvement or were becoming worse under conservative treatment. The trauma of hip fracture tipped the balance in these elderly people in much the same manner that a bronchopneumonia becomes the terminal event in the elderly patient with cardiac disease. Seventeen patients fell into this group; 9 were operated upon, and 8 were treated conservatively; all died. The following case is typical:

H. E., a 77-year-old woman, entered the hospital on January 21, 1945. On the day of admission she had tripped and fallen on her right hip, sustaining a fracture of the right femoral neck. Physical examination showed an elderly, unco-operative woman in moderate pain. The lungs demonstrated bilateral moist rales at the bases. The cardiac border extended to the left, the sounds were of poor quality, and there were rough systolic murmurs at both apex and base. The peripheral arteries showed evidence of marked arteriosclerosis, and the eyegrounds consistent changes. The blood pressure was 160/110. There was shortening and external rotation of the right leg. The urine was normal. Examination of the blood disclosed a hemoglobin of 57 per cent and a white-cell count of 7200. The blood Hinton reaction was negative. The nonprotein nitrogen was 43 mg., and the fasting blood sugar 110 mg. per 100 cc.

The patient was placed in Russell traction. When seen by a medical consultant shortly after admission she was found to be in marked congestive failure. She was placed on a salt-poor diet and given ammonium chloride, mercupurin, digitalis and sulfadiazine. She did not improve under this regimen and became more and more unco-operative. Her course was downhill, cardiac failure persisting. A bronchopneumonia developed, and she died on the 22nd hospital day.

In our opinion operation would not have changed the outcome in this case.

TABLE 2. *Conditions Existing before Operation in 72 Cases.*

CONDITION	NO. OF CASES	SURVIVALS*	DEATHS†
Cardiovascular disease	41	31	10
Decubitus ulcer	9	8	1
Renal-tract infection	8	8	0
Anemia (severe)	7	7	0
Diabetes	7	4	3
Pneumonia	6	5	1
Previous cerebrovascular accident	6	6	0
Psychosis	6	4	2
Emphysema (pulmonary)	5	4	1
Prostatism	5	5	0
Cataracts	4	4	0
Urinary and fecal incontinence	3	3	0
Bronchiectasis	2	2	0
Obesity	2	2	0
Carcinoma of stomach	2	1	1
Colles fracture	2	2	0
Bilateral active pulmonary tuberculosis	1	1	0
Uremia and acidosis	1	0	1
Hypoproteinemia (severe)	2	1	1
Cachexia (extreme)	1	1	0
Rheumatoid arthritis	1	1	0
Reticulum-cell sarcoma of pelvis	1	1	0
Pernicious anemia	1	1	0

*Total of 59 cases.
†Total of 13 cases.

Table 2 lists the recorded underlying diseases that, in various combinations, were found in the 72 patients undergoing operation. It is immediately apparent that cardiovascular disease was the greatest complicating factor. Forty-one cases were diagnosed as either arteriosclerotic heart disease or hypertensive heart disease, or both. No cases of rheumatic or syphilitic heart disease were encountered, as might be anticipated in this age group. Ten of these 41 patients were in congestive failure. Other medical disabilities having a direct effect on the outcome were diabetes, pneumonia, uremia and psychoses.

Table 3 demonstrates the effect of congestive failure on the mortality and points out that the mere presence of cardiac disease has little or no bearing on the general mortality rate, provided there is no failure.

TABLE 3. *Arteriosclerotic and Hypertensive Heart Disease in 41 Patients Operated Upon.*

STATUS	NO. OF CASES	SURVIVALS	DEATHS
Compensated	28	26	2
Congestive failure	13	5	8
Totals	41	31	10

Table 4 lists the complications following surgery. Conditions existing prior to surgery are not included in this list. Noteworthy is the high incidence of pulmonary complications such as pneumonia, atelectasis and emboli. Circulatory failure developed in only 3 cases.

TABLE 4. *Complications Following Operation.*

COMPLICATION	TOTALS	SURVIVALS	DEATHS
Pneumonia	10	4	6
Phlebothrombosis or thrombophlebitis, or both	11	9	2
Pulmonary embolism	2	0	2
Atelectasis	3	2	1
Circulatory failure (shock)	3	0	3
Uremia	2	0	2
Renal-tract infection	4	4	0
Cerebrovascular accident	1	0	1
Ileus	3	1	2
Wound infection	4	4	0
Gangrene of involved extremity	2	0	2
Psychosis	3	2	1
Decubitus ulcer	7	5	2
Gastrointestinal hemorrhage (carcinoma of stomach)	1	0	1

DISCUSSION

Preoperative Study

In medical evaluation certain points in the history and physical examination are of special concern.

History. One should determine, in eliciting the present illness, whether the trauma was a result of a simple accident, such as tripping or slipping, or whether the patient fell because of a "fainting spell." In this age group such spells are often due to serious

underlying disease involving the cardiovascular system.

In senescence degenerative changes take place throughout the body, leaving the various organ systems prone to breakdown at periods of stress and strain. Special attention should be given to symptoms referable to the cardiovascular, renal and pulmonary systems. Evaluation of cardiac cases depends a great deal on the history. This has been emphasized by Sprague,[9] who points out that the history is of more importance than the stethoscope or electrocardiogram. Patients who have led normal, active lives with no symptoms of cardiac failure will offer no cardiac problem to the surgeon. On the other hand, patients whose activities have been restricted because of dyspnea or chest pain may be hazardous surgical risks. Dyspnea or cough may also indicate decreased pulmonary reserve. Renal disease may be manifested only by a history of polyuria or nocturia.

Physical examination. Mere inspection of the patient tells a great deal. Is the patient oriented? Disorientation is often the only manifestation of a cerebrovascular accident. Shock, which is present in all cases to a greater or lesser degree, may cause mild to severe changes. The patient who is oriented and who lies flat in bed in traction with no increase in respiratory rate will usually prove a good surgical risk.

An enlarged heart or the presence of murmurs in no way contraindicates surgery provided cardiac compensation is present. Cardiac rhythm is of special concern. Such arrhythmias as auricular fibrillation and premature ventricular systoles demand special attention and treatment.

Adequate examination of the lungs is difficult in these cases. The finding of rales is usually ominous. They may be due to shock or myocardial failure, or both, and may indicate hypostatic changes with infection. All these conditions require prompt, adequate treatment.

Abdominal distention is occasionally seen after hip fracture. Causes such as incipient intestinal obstructions, uremia and cerebrovascular accident should be considered alongside post-traumatic ileus.

Laboratory data. The following studies are recommended: complete urinalysis, hemoglobin determination, red-cell count, white-cell count and differential, blood nonprotein nitrogen, fasting blood sugar and blood carbon dioxide combining power. An electrocardiogram is often indicated.

Evaluation of the patient as a surgical risk will frequently require twenty-four to forty-eight hours or longer. During this period shock is corrected, fluid balance is established, and the patient is placed in optimum condition to withstand operation. On the basis of the history, physical examination, laboratory studies and response to therapy the patient can be classified in one of the three groups proposed. Only patients in Group III should be refused operation. If a patient is becoming worse under adequate medical management in traction, we do not believe that operation will in any way alter the course for the better. On the contrary, it will undoubtedly hasten death.

Cardiovascular Factors

The incidence of cardiovascular disease, of either the hypertensive or the arteriosclerotic type, is notably high in elderly patients. Their cardiac reserve is low, and they are easily thrown into congestive failure or shock by the altered circulatory dynamics following the trauma of hip fracture. No operation should be attempted on such patients until the cardiac failure has been corrected. Once this has been accomplished, no type of heart disease except recent myocardial infarction is a contraindication to hip nailing.

The routine use of digitalis in patients who are not in failure should be avoided, since it decreases cardiac output and increases the irritability of the myocardium and hence predisposes to the development of ventricular tachycardia or fibrillation. If there is any evidence of ventricular irritability, such as ventricular extrasystoles, the patient should be given 0.2 to 0.3 gm. (3 to 5 gr.) of quinidine every four hours. This drug is efficacious in preventing fatal cardiac arrhythmias that might develop during operation.

The vascular degenerative changes in the aged predispose to shock as a result of trauma. The widespread arteriosclerosis — and, therefore, the diminished elasticity and adaptability of the vascular system — does not permit the compensatory changes seen in the younger age group. Because of this, shock must be treated as early and as adequately as possible. This lowered capacity of the vascular system for adaptation should be kept in mind when fluids are administered intravenously, for a sudden increase in circulatory volume in these patients may be fatal.

The danger of arterial thrombosis is ever present. Although the occurrence of massive myocardial infarction is not common in the aged, there may be extensive small thromboses in branches of the main coronary arteries, and in spite of lack of chest pain and electrocardiographic changes, the patient may die of coronary-artery insufficiency. Thrombosis of arteries in the brain may be accompanied by no peripheral neurologic signs, the only manifestation of this catastrophe being a change in character or sensorium, abdominal distention or, worse, the development of a frank psychosis. Shock by slowing of the blood flow enhances the possibility of thrombosis in this age group.

Eleven of the patients operated on showed signs and symptoms of thrombophlebitis or phlebothrombosis. In these cases pulmonary emboli developed in 2, who died. This is a rather low figure, and it is quite possible that patients believed to have pneu-

monia have had pulmonary emboli from silent thromboses in the legs. It is important to realize that in the aged the manifestations of peripheral venous thrombosis and pulmonary embolization may be minimal and may be unrecognized unless sought for quite diligently.

Pulmonary Factors

Although failure of the cardiovascular system predominated as a cause of death, pulmonary complications were of importance (Table 4). Just as the vascular system becomes inelastic, so also does the thoracic cage. The costal cartilages become calcified, and changes occur in the intervertebral disks of the thoracic spine, with ensuing deformities that contribute to the rigidity of the chest wall and lead to emphysema. The net results are poor respiratory mechanics, with improper drainage of the bronchial tree and thus a predisposition to pneumonia and atelectasis. Hence one must expect and try to prevent the occurrence of these complications. An expectorant such as potassium iodide may be used to thin out the bronchial secretions and prevent obstruction of bronchi with tenacious plugs of mucus. Deep breathing should be encouraged, and as much painless motion as possible in traction should be instituted. Exposure of the patient to upper respiratory infection should be scrupulously avoided. The use of penicillin both before and after operation has been of tremendous help in the prevention and treatment of lung infection.

Renal Factors

Renal factors deserve special attention in the elderly age group. Shock[10] has shown in a study of elderly men that inulin clearance, a measure of glomerular filtration, is 60 per cent of normal, whereas Diodrast clearance, which gives a more complete over-all picture of kidney function, is decreased to 45 per cent of normal. The recent work of Trueta et al.[11] in demonstrating the renal shunt mechanism following fractures of extremities and other noxious stimuli makes it evident that trauma, with its concomitant shock, may further decrease renal function to the point of serious decompensation. We have found that operation on a patient with an elevated or rising nonprotein nitrogen can have disastrous results. Of similar importance is the carbon dioxide combining power of the blood. One of the prime functions of the kidney is the regulation of the acid-base equilibrium of the body. It does this by a process of selective retention or excretion of various salts. An early manifestation of impaired function is often a loss of this fine discriminatory power. As a result there is a retention in the body of sulfates and phosphates at the same time that there is a loss of fixed base. This can lead to a rather severe acidosis, which must be corrected prior to operation. If the nonprotein nitrogen is high or the carbon dioxide low, the condition is corrected preoperatively by the use of fluids, sodium lactate or bicarbonate and saline solution as indicated. If there is no chemical improvement or still further deterioration, operation should not be performed.

Renal-tract infection was seen in 10 of the 72 patients operated on either before or after surgery. It is important to maintain an adequate urine flow both in the prevention and in the treatment of this condition. In men urinary retention secondary to prostatic obstruction must be avoided, and constant drainage should be instituted whenever there are signs and symptoms of such a difficulty.

Complete studies on water and electrolyte balance have been presented by Maddock and Coller.[12, 13] Sufficient fluid should be administered either by mouth or parenterally to maintain a urine output of 1000 to 1500 cc. daily.

Diabetes Mellitus

There were 7 diabetic patients in the group. Of these, 3 died. As a rule the elderly patient with diabetes of long standing presents a hazardous problem to both the surgeon and the internist. McKittrick[14] has pointed out the necessity of more deliberate and careful preparation for operation on patients with diabetes. The 3 fatal cases were never well controlled, and the patients showed elevated blood sugars and continually lost large amounts of sugar in the urine. In 2 cases gangrene of the involved limb occurred, and all 3 patients succumbed to overwhelming infection.

Summary

A study of 100 patients over the age of seventy admitted to the Boston City Hospital with hip fractures revealed a significant number with preexisting medical disabilities. A grouping of the cases according to type and severity of such disabilities and the response to medical therapy is presented. Group I comprised good surgical risks, Group II fair risks, and Group III patients on whom operation was contraindicated. The effect on the mortality rate of degenerative diseases in the cardiovascular, pulmonary and renal systems and the management of these diseases are discussed.

References

1. Hershey, S. G., and Apogi, E. Anesthetic management of aged patients with fractured neck of femur. *New York State J. Med.* **44**: 183-188, 1944.
2. O'Brien, R. M., Shy, J. C., and Bublis, N. J. Internal fixation of trochanteric fractures of femur; report of 103 consecutive cases. *J. Bone & Joint Surg.* **28**:791-797, 1946.
3. Stuck, W. G. Treatment of intertrochanteric fractures of femur. *Surgery* **15**:275-291, 1944.
4. Swart, H. A., and Miyakawa, G. Fractures of femur: results of treatment of 179 patients. *Am. J. Surg.* **65**:221-225, 1944.
5. Linton, P. On different types of intracapsular fractures of femoral neck: surgical investigation of origin, treatment, prognosis and complications in 365 cases. *Acta Chir. Scandinav.* **90**:(Supp. 86), 1-122, 1944.
6. Cleveland, M. Critical survey of ten years' experience with fractures of neck of femur. *Surg., Gynec. & Obst.* **74**:529-540, 1942.
7. Taylor, G. M., Neufeld, A. J., and Janzen, J. Internal fixation for intertrochanteric fractures. *J. Bone & Joint Surg.* **26**:707-712, 1944.

8. Leydig, S. M., and Brookes, T. P. Treatment of pertrochanteric fracture of femur with lag bolt. *J. Missouri M. A.* **37**:354-357, 1940.

9. Sprague, H. B. Normal senile heart and diagnostic problems. In *Geriatric Medicine: Diagnosis and management of disease in the aging and in the aged.* Edited by E. J. Stieglitz. 887 pp. Philadelphia: W. B. Saunders Co., 1943. Pp. 371-388.

10. Shock, N. W. Kidney function in aged males. *Geriatrics* **1**:232-239, 1946.

11. Trueta, J., et al. *Studies of the Renal Circulation.* 187 pp. Springfield, Ill.: Charles C Thomas, 1947.

12. Maddock, W. G., and Coller, F. A. Water balance in surgery. *J. A. M. A.* **108**:1-6, 1937.

13. Coller, F. A., and Maddock, W. G. Water and electrolyte balance. *Surg., Gynec. & Obst.* **70**:340-354, 1940.

14. McKittrick, L. S. Recent advances in care of surgical complications of diabetes mellitus. *New Eng. J. Med.* **235**:929-932, 1946.

ACUTE HERPETIC GINGIVOSTOMATITIS IN THE ADULT*

ARTHUR M. ROGERS, M.D.,† LEWIS L. CORIELL, PH.D., M.D.,‡ HARVEY BLANK, M.D.,§ AND THOMAS F. McNAIR SCOTT, M.D.¶

PHILADELPHIA

THE majority of people, about 70 per cent, experience their first infection with the herpes simplex virus in infancy or early childhood. This infection is usually inapparent, and can therefore only be recognized as having occurred by the presence of circulating antibodies.[1] However, in about 1 per cent of all infections, the first attack of the virus can give rise to a serious or even fatal disease. These primary infections, of which the commonest is the clinical entity known as acute herpetic gingivostomatitis,[2-6] are well recognized in childhood because they commonly occur in this age group. In adult life, however, these clinical manifestations, on the basis of the figures just quoted, rarely occur and therefore are liable to go unrecognized as herpetic infections. The common adult manifestation of infection is recurrent herpes labialis or "fever blisters." These recurrent attacks are usually accepted as being due to a reactivation, by nonspecific stimuli, of the herpes virus that has lain latent in the tissues of the host since recovery from the primary infection, whether clinical or inapparent.

In view of these facts, it seems worth while to record the clinical picture of primary herpetic infection that occurred in 3 adult patients.

Youmans,[7] in 1932, reported the first case in an adult in which the virus was isolated. Long[8] described 3 cases with the isolation of the virus from two. Scott, Steigman and Convey[9] observed a primary infection in a mother whose children were being treated for the same disease; in addition to isolating the virus, the authors demonstrated the development of neutralizing antibodies during convalescence. Scott[10] discussed another case in a soldier in England from whom the virus was isolated, and the development of antibodies was demonstrated during convalescence. Ziskin and Holden[11] reported 8 cases of acute herpetic gingivostomatitis in adults, and Florman and Trader[12] a case in an adult. In all these cases the clinical impression was corroborated by laboratory findings.

CASE REPORTS

CASE 1. A 21-year-old secretary was admitted to the Hospital of the University of Pennsylvania on December 3, 1947, complaining of sore mouth and fever. Her illness had begun 2 days previously, when she had discovered, on brushing her teeth, that the gums were extremely painful. She felt a little nauseated. For the next 2 days she felt chilly and feverish, and her gums became progressively worse. A slight headache developed, but there was no stiffness of the neck.

The patient had never previously had a cold sore or "canker sores." Her mother had typical herpes labialis at the onset of the patient's illness.

Since the patient was later found to have infectious mononucleosis, in addition to the herpes simplex infection, some further details about two febrile illnesses that occurred in the month preceding the onset of the present illness are presented. On November 1 a running nose, sore throat, and backache developed, and the patient was sick, with a fever, for 4 days. Her temperature reached a maximum of 102°F. She recovered and returned to work until November 14, when a sore throat and fever of 4 days' duration occurred; the temperature rose to a maximum of 102°F. During this illness, she was under the care of her family physician, who made a diagnosis of acute tonsillitis and treated her with sulfadiazine. When seen by one of us (A.M.R.) in consultation on November 17, she had a temperature of 100°F., and was feeling much better than she had for the previous 2 days. Her pharynx was moderately inflamed, and both tonsils were enlarged and partially covered with a gray-white exudate. No blood counts or other laboratory studies were done at this time. She recovered from this illness and returned to work on November 24, working regularly until the day of admission.

Physical examination revealed that the breath was foul; the gums were swollen and inflamed, especially along the gingival margins, and bled easily on manipulation; inside the lower lip at the angle of the mouth were two aphthous ulcers, and many unruptured small blebs were scattered throughout the buccal mucosa. On the left buccal mucosa there was a white, desquamating patch, 1 cm. in diameter. The submaxillary and posterior cervical lymph nodes were enlarged and tender. No other lymph nodes were enlarged. The spleen was not palpable.

The temperature was 103.4°F.

Examination of the blood showed a hemoglobin of 81 per cent and a white-cell count of 6100, with 53 per cent neutrophils, 21 per cent monocytes, 24 per cent lymphocytes, 1 per cent eosinophils and 1 per cent basophils. No immature cells were seen. On December 6 an essentially similar count was obtained except that a few immature atypical lymphocytes were noted. Urinalysis on three occasions was negative. A gingival smear for Vincent's organisms taken on the day of admission was negative, and a throat culture revealed a normal flora. Blood drawn for heterophil-antibody tests on December 6 revealed a titer of 1:5096, which was reduced to 1:448 after absorption with guinea-pig antigen, and was completely absorbed by beef-cell antigen.

*From The Children's Hospital and the departments of Medicine, Pediatrics and Dermatology of the University of Pennsylvania School of Medicine.

Aided by grants from the Lederle Laboratories, American Cyanamid Company, and the National Foundation for Infantile Paralysis.

†Associate in medicine, University of Pennsylvania School of Medicine.

‡Senior fellow in virus research, National Research Council.

§Fellow in the medical sciences, National Research Council.

¶Research professor of pediatrics, University of Pennsylvania School of Medicine; director of research and clinics, Children's Hospital.

The mouth lesions increased in severity, and on December 6, 51 distinct aphthous ulcers were counted on the uvula, tongue, buccal mucosa, gingiva and hard palate. They were equally distributed on both sides. Enlarged and tender submental lymph nodes were noted at this time. The temperature became normal on the 8th day of illness, and the patient was discharged to her home. She reported on December 11 that she had only three unhealed lesions. When she was seen on December 15 no lymphadenopathy was present, and the oral mucous membranes were normal except for a slight redness along the gingival margins, which had disappeared by December 29.

In February, 1948, the patient complained of painful, bleeding gums for a week. In March an aphthous ulcer appeared on the buccal mucosa, but the virus of herpes simplex could not be isolated at this time, and a biopsy of the ulcer showed no typical inclusion bodies. Since then the patient has had no trouble with her mouth.

The diagnosis of herpetic stomatitis was confirmed by three methods: isolation of the virus of herpes simplex from the oral lesions; biopsy of one of the mouth lesions; and demonstration of neutralizing antibodies in the convalescent serum that were absent in the serum taken at the onset of the disease.

On December 4, 1947, saliva was collected and, after treatment with penicillin and streptomycin, was inoculated onto the chorioallantoic membrane of embryonated hens' eggs. Subsequent examination of the membrane showed numerous plaques similar to those produced by the virus of herpes simplex. The virus was propagated serially in eggs, and was specifically neutralized by rabbit antiserum for the HF strain of herpes simplex virus. Biopsy of one of the ulcers of the patient's mouth was taken on December 4, 1947. In the microscopical section stained with hematoxin and eosin, balloon-

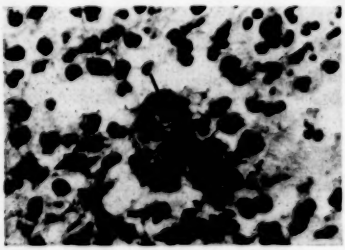

FIGURE 1. *Biopsy of Aphthous Ulcer of the Buccal Mucosa in Case 1.*

Three swollen epithelial cells containing herpetic inclusion bodies that completely fill the nucleus are surrounded by an inflammatory exudate (hematoxylin and eosin stain x 300).

ing cells containing intranuclear inclusion bodies typical of herpes simplex infection were seen in the epidermis (Fig. 1). Neutralization tests were carried out on the egg membranes with the HF strain of herpes-simplex virus and the patient's acute and convalescent serums. No neutralizing antibodies were present in the serum drawn on December 4, whereas the 1:16 dilution of serum drawn on December 15 completely neutralized the standard strain of herpes simplex virus.

CASE 2. E. C., a 34-year-old housewife, was seen at home on September 20, 1947, with the chief complaint of "sore mouth," headache, backache and malaise of 1 day's duration. She dated the onset of the sore mouth and gums from the previous day, when she had massaged her teeth and gums vigorously. She had never had a cold sore in her life, although her husband had frequent cold sores and was recovering from a recent attack at the time.

Physical examination showed the anterior cervical lymph nodes to be swollen and tender; the gums were slightly swollen and red, especially along the gingival margin. On the following day the temperature was 100°F., the gums were more swollen and more inflamed, and several aphthous ulcers were seen inside the lower lip, on the tongue and on the gingiva. Several grouped vesicles were seen on the lips at the left angle of the mouth. The malaise, fever and sore mouth persisted for 1 week. On September 30, a few healing ulcers were still visible on the gingiva and lips, although there was no subjective pain at this time.

The temperature by mouth was 99.1°F.

Gingival smears were made for Vincent's organisms on September 21, 26 and 30; all were negative. A culture of the gingiva on September 21 revealed no abnormal bacteria. From saliva collected on September 23, herpes-simplex virus was isolated in chick embryos. Serums taken during the acute and convalescent stage of the disease showed a rise in titer of neutralizing antibodies for herpes simplex from 0 to 1:16.

CASE 3. A 1st-year medical student noted the onset of his illness on April 22, 1948, when the submental and submaxillary lymph nodes became tender and swollen. On the following day, the gums were sore, and he began to feel chilly and feverish intermittently. For the next 4 days the soreness

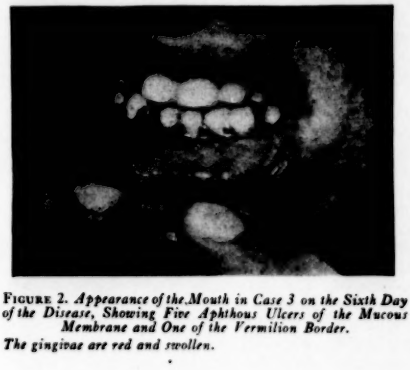

FIGURE 2. *Appearance of the Mouth in Case 3 on the Sixth Day of the Disease, Showing Five Aphthous Ulcers of the Mucous Membrane and One of the Vermilion Border.*

The gingivae are red and swollen.

of the gums progressed and involved the cheeks, tongue and throat. He was admitted to the Student Health Service of the University of Pennsylvania with an oral temperature of 100°F. and a pulse of 90.

Physical examination revealed a moderate bilateral cervical adenopathy, with ulcerations on the lips, buccal mucosa, tongue and tonsils (Fig. 2). A palpable lymph node was felt in the left axilla. No other nodes were enlarged. The spleen was not felt.

The urine was normal. Examination of the blood disclosed a white-cell count of 8000, with 71 per cent neutrophils, 26 per cent lymphocytes and 3 per cent monocytes. The temperature rose to a maximum of 100.6°F., and then gradually subsided over the next 4 days, reaching normal on the 9th day of the disease. The mouth lesions continued to progress and became worse until the 8th day of the disease. From then on, the healing was quite rapid. On April 28 a heterophil-antibody test was negative, as was a serologic test for syphilis. Neutralizing antibodies against the herpes-simplex virus were absent from the serum taken on the 7th day of the disease, but present in serum drawn 2 weeks later.

DISCUSSION

The clinical features of the 3 cases presented are similar to those previously reported in both children

and adults. No patient gave a history of previous fever blisters or canker sores, and in 2 cases recent contact with a person who had a cold sore suggested a likely source of infection. The chief complaint of the 3 patients was sore mouth, fever and malaise. Inspection of the oral cavity revealed in some cases vesicular lesions, but chiefly many small, shallow discrete ulcers measuring 1 to 5 mm. in diameter. The gingivae were acutely inflamed along the margin. Ulcerations were frequently present on the alveolar and palatal gingivae. The regional lymph nodes were uniformly enlarged. The temperature varied from 100 to 103°F. by mouth, returning to normal during the course of a week. New lesions kept appearing in the mouth during the first few days, and remained painful throughout the first week. Healing gradually occurred during the second week, without scarring.

In the 2 cases so examined, the total white-cell count was not elevated. Except in the patient who was recovering from infectious mononucleosis, the differential counts were normal. In the 3 cases reported by Long,[8] the white-cell and differential counts were within normal limits.

The diagnosis of infection with herpes-simplex virus was confirmed in each case by the demonstration of the development of specific neutralizing antibodies during convalescence. In 2 cases the herpes-simplex virus was recovered from saliva, and typical inclusion bodies were seen in sections of biopsy material in 1.

The sudden onset of fever, sore mouth and regional adenopathy in a previously healthy adult immediately presents a problem of differential diagnosis. The diagnostic probabilities include Vincent's infection, or trench mouth, erythema multiforme, infectious mononucleosis, syphilis, agranulocytosis, acute leukemia, pemphigus vulgaris and diphtheria of the pharyngeal or tonsillar region.

A negative peridontal smear for organisms of the Plaut–Vincent type is helpful, but a positive smear is of no value because these organisms are frequent in normal mouths, and more frequent in the presence of acute inflammation when pain prevents proper cleansing and oral hygiene. Burket[10] and Ziskin and Holden[11] stress ulceration of the interdental papilla as the typical lesion of acute Vincent's infection, and in severe cases they describe ulcerations covered by a gray or yellow pseudomembrane on the palatal, buccal and labial mucosa. The fusospirochetal infection can be controlled by penicillin therapy, which does not shorten the course of the herpetic gingivostomatitis.

The treatment is symptomatic. The use of tetracaine hydrochloride 1 per cent (Pontocaine Hydrochloride) or p-amino-benzoyl-dibutyl-aminopropanol sulfate 2 per cent (Butyn Sulfate) locally before meals affords much comfort. The intense soreness of the gums makes brushing of the teeth impossible, so that irrigation of the mouth is essential. We have used benzalkonium chloride 1-1000 (Zephiran) or cetylpyridinium chloride 1-4000 (Ceepryn) for that purpose. Penicillin should be used to control secondary infection by fusospirochetal organisms or pyogenic cocci.

Recurrent fever blisters are generally accepted to be manifestations of a recrudescence of a latent herpes-simplex virus, but there is no laboratory evidence that recurrent aphthous ulcers are caused by this virus. It is interesting to note that one of the patients did have a "canker sore" for the first time in her life after recovery from the primary infection. However, no herpes virus was recovered, nor were the inclusion bodies seen in a biopsy specimen of this lesion.

Levine et al.[11] reported, as probably herpetic in origin, an epidemic of vesicular pharyngitis and stomatitis that involved almost 50 per cent of 230 people in a summer camp. Recent knowledge of the epidemiology and clinical manifestations of herpes indicates that this epidemic was not due to infection with the virus of herpes simplex for the following reasons: most people over three to five years of age have already contracted a primary infection and are immune to reinfection from without; vesicles, rarely observed in herpetic gingivostomatitis, were "present in *all* the epidemic cases"; the ulcers were "grayish yellow," in contrast to the whitish ulcers of herpes; and some of the most consistent findings in herpes infection—marginal gingivitis, pain and regional lymphadenopathy—were minimal or present in less than half the epidemic cases. We have observed a small epidemic of the syndrome described by Levine et al. and were unable to isolate a virus or to demonstrate a rise in neutralizing antibodies for herpes simplex during convalescence.

Summary

Three cases of acute herpetic gingivostomatitis in adults are reported. The clinical picture is described, and its similarity to the disease in infants is noted—namely, an acute, febrile illness with malaise, chilliness, multiple aphthous ulcers of the mouth and pharynx, marginal gingivitis and regional-lymph-node enlargement.

The methods by which a positive diagnosis may be established in the laboratory are illustrated: isolation of the virus; demonstration of typical inclusion bodies in a biopsy specimen; and the appearance of specific neutralizing antibodies in the serum during convalescence.

References

1. Andrewes, C. H., and Carmichael, E. A. Note on presence of antibodies to herpes virus in post-encephalitic and other human sera. *Lancet* **1**:857, 1930.
2. Dodd, K., Buddingh, J., and Johnston, L. Herpetic stomatitis: enanthem. *Am. J. Dis. Child.* **58**:907, 1939.
3. Dodd, K., Johnston, L. M., and Buddingh, G. J. Herpetic stomatitis. *J. Pediat.* **12**:95-102, 1938.
4. Burnet, F. M., and Williams, S. W. Herpes simplex: new point of view. *M. J. Australia* **1**:637-642, 1939.
5. Parsons, C. G. Stomatitis in childhood. *Arch. Dis. Child.* **15**:43-54, 1940.

6. Black, W. C. Etiology of acute infectious gingivostomatitis (Vincent's stomatitis). *J. Pediat.* **20**:145-160, 1942.
7. Youmans, J. B. Herpetic fever with stomatitis; report and discussion of case in which virus was isolated. *South. M. J.* **25**:228-233, 1932.
8. Long, P. H. Herpetic pharyngitis and stomatitis: report of three cases. *J. Clin. Investigation* **12**:1119-1125, 1933.
9. Scott, T. F. M., Steigman, A. S., and Convey, J. H. Acute infectious gingivostomatitis: etiology, epidemiology and clinical picture of common disorder caused by virus of herpes simplex. *J. A. M. A.* **117**:999-1005, 1941.
10. Scott, T. F. M. Unpublished data.
11. Ziskin, D. E., and Holden, M. Acute herpetic gingivostomatitis: report of fifteen cases. *J. Am. Dent. A.* **30**:1697-1705, 1943.
12. Florman, A. L., and Trader, F. W. Comparative study of pathogenicity and antigenicity of four strains of herpes simplex. *J. Immunol.* **55**:263-275, 1947.
13. Burket, L. W. *Oral Medicine: Diagnosis, treatment.* 674 pp. Philadelphia: J. B. Lippincott Co., 1946.
14. Levine, H. D., Hoerr, S. O., and Allanson, J. C. Vesicular pharyngitis and stomatitis: unusual epidemic of possible herpetic origin. *J. A. M. A.* **112**:2020-2022, 1939.

RADIATION EXPOSURES FROM THE USE OF SHOE-FITTING FLUOROSCOPES

CHARLES R. WILLIAMS, PH.D.*

BOSTON

IT IS now common practice in many shoe stores and shoe departments of department stores to supplement usual shoe-fitting methods by the use of fluoroscopes known as x-ray shoe fitters. Because this technic has spread rapidly throughout the United States, particularly in stores specializing in children's shoes, it is desirable to know precisely the exposures to irradiation received by customers, as well as by clerks and other persons in the area of x-ray shoe-fitting units.

For this reason a series of studies was undertaken for the purpose of measuring foot dosage, leakage through the walls of the cabinet and scattering from the opening in which the customer places his feet. The data obtained form the basis of this report.

EQUIPMENT

The unit consists essentially of a 50-kv. x-ray tube operating at 3 to 8 milliamperes through a 1-mm. aluminum filter, housed in a case lined with lead or steel and containing a fluorescent screen. The focal spot to skin distance is 7.5 to 20 cm. The unit is equipped with an opening for the customer's feet and three viewing openings through which the customer, clerk and one other person can observe the screen. A push-button automatic timer, which can be set for any predetermined time, is included on most installations. In actual use exposure times have been found to vary from five to forty-five seconds, although twenty seconds appears to be the most popular setting. *Repeated exposures can be made by releasing and pushing of the button.* More recent models are equipped with three separate switches providing three different intensities — one for men, one for women and one for children.

FOOT DOSAGE

The amount of radiation delivered to the feet of the customer is a quantitative matter related to tube output, focal skin distances and time of exposure. A large series of measurements (on 12 units) using a Victoreen r-meter placed inside a shoe showed wide variations in the quantity of radiation delivered to the feet.

Figure 1 shows dosage curves for several typical units. Total exposure values were determined for a series of time settings on each shoe-fitter. By the plotting of total r against time the results establish a straight line from which dosage rate can

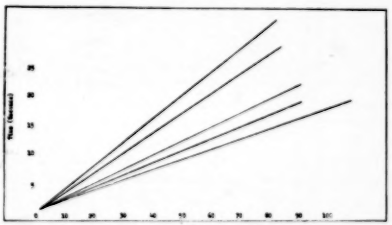

FIGURE 1. *Foot Dosage in Shoe-Fitting Fluoroscope. The timer is normally set for twenty to twenty-two seconds.*

be derived. All installations tested fall within the range of the curves shown — that is, from 0.5 to 5.8 r per second. By multiplying total exposure time and dosage rate, one can determine the total foot dose per exposure. Thus, for a twenty-second exposure (that most commonly used) doses ranging from 10 to 116 r could be delivered to the feet of a customer. Repeated fittings increase the exposure in proportion to time.

SCATTERED RADIATION

This is defined in the American Standards Association Code (Paragraph 3-2.1.3)[1] as "radiation which during passage through a substance, has been deviated in direction and also may have been modified by an increase in wavelength." The foot opening in shoe-fitting units is the most important source of radiation of this type. After passing

*Assistant professor of industrial hygiene, Harvard School of Public Health.

through the aluminum filter and the customer's feet it escapes from the cabinet through the opening. In most installations this amounts to more than 100 milliroentgens (mr) per hour at 10 feet from the unit and 15 mr per hour at 25 feet. The zone of scattered radiation in excess of 15 mr per hour covers an area of about 90° from the foot opening out into the room.

Figure 2 shows a typical setup in a shoe store. It should be noted that at many of the seats where customers are given preliminary fittings, an area in which clerks may be working, a total daily dose

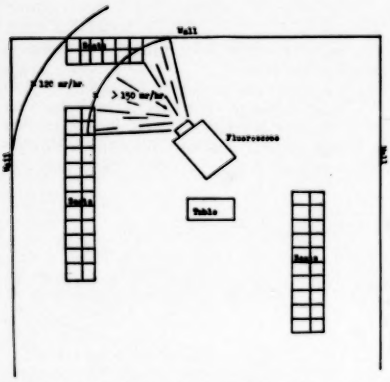

FIGURE 2. *Distribution of Scattered Radiation from Shoe-Fitting Fluoroscope.*

could be received in one hour of operation by anyone in the area.

CABINET–WALL LEAKAGE

Measurements of leakage directly through the walls of the cabinets showed wide differences between units. These differences varied with manufacturer, age and condition of the equipment and condition of the x-ray tube.

Values were obtained using two rate meters — a Zeus survey meter with a range of 0 to 2500 mr per hour and a Victoreen radiation meter having a range of 0 to 2.0 mr per minute (0 to 120 mr per hour). Readings were taken at the sides, front, back and in the zone where viewing is done. The front of the machine is the side on which the control buttons are located, the back is where the customer stands. It should be noted that values found on the back are influenced by scattering from the opening where the feet are placed.

It can be seen from Table 1 that there is some leakage directly through the walls of the cabinets. The figures represent the dosage rates received by persons adjacent to the cabinet. They can be evaluated in terms of the permissible daily dose of 100 milliroentgens (12 mr per hour) as established by the American Standards Association.[1] The length of time for which a person can be in close proximity to one of these units can be determined by comparison of the leakage (rate) with the permissible

TABLE 1. *Leakage through Walls of Shoe-Fitting Fluoroscope.**

SITE OF LEAKAGE	NO. OF UNITS	AMOUNT OF LEAKAGE		
		BOTTOM	MIDDLE	TOP
		mr/hr.	*mr/hr.*	*mr/hr.*
Front	12	3 to 6	12 to 48	12 to 36
Sides	12	7 to 60	12 to 36	8 to 24
Back	12	200	30 to 100	6 to 54
Viewing position	12	Values range from 0 to 24 mr per hr.		

*Taken at the walls.

daily dose. The leakage must be measured for each unit.

CONTROL OF EXPOSURE

There are many steps that should always be taken in the use of this equipment to minimize exposures to customers and clerks. Each unit must be treated as an individual problem.

Foot dosage. The control of foot dosage depends on four factors: the output of the tube, thickness and condition of filters, distance, time of exposure and number of exposures. The control of the first two rests with the manufacturer, and that of the last two with the store.

The American Standards Association[1] and the New York City Health Department[2] have specified that "The maximum permissible dose per exposure shall not exceed 2 roentgens." New York City requires further that "There shall not be more than 3 exposures in one day and not more than a total of 12 exposures in one year." The only attempt to enforce this provision is a requirement for posting of signs on the machines stating: "REPEATED EXPOSURES TO X-RAYS MAY BE HARMFUL. FLUOROSCOPIC EXAMINATIONS FOR SHOE FITTING SHOULD BE LIMITED TO NO MORE THAN 12 IN ONE YEAR." These signs should measure at least 7½ inches by 4½ inches and should be posted conspicuously.

More recent proposals by the Bureau of Industrial Hygiene, Detroit Department of Health,[3] require that maximum intensity in the beam shall not exceed 12 mr per minute and that maximum time of exposure shall not exceed five seconds. The same dose limit is being recommended by the Division of Occupational Hygiene of the Massachusetts Department of Labor and Industries. Based on this figure, suggested warning signs state that the

limit for each customer shall be 3 x-ray shoe fittings per day, and no more than 12 fittings per year.

These figures indicate the exposure levels now being established by municipal and state authorities in their regulations to control the use of shoe-fitting fluoroscopes.

Scattered radiation and wall leakage. Leakage through the walls of the equipment can be controlled only by the manufacturers, since it depends on shielding in the cabinet and the tube output.

Control of scattered radiation is the responsibility of the user because the controlling factor is the position of the unit with respect to occupied areas.

The New York City Sanitary Code (Section 107a) specifies under Regulation 2 that — "The equipment shall be so constructed that the dosage rate in any region which may be occupied by operators and attendants does not exceed 12.5 milliroentgens per hour." It is obvious from the data shown in the section on scattered radiation that the back (customer's) side of these units should never be directed toward occupied areas within a radius of 25 feet.

Summary

Measurements on shoe-fitting fluoroscopes in use show that foot dosages may range from 0.5 to 5.8r per second (time of exposure five to forty-five seconds), that wall leakage may range from 3 to 60 mr per hour and that scattered radiation amounts to more than 100 mr per hour at distances up to 10 feet from the unit.

References

1. *Safety Code for the Industrial Use of X-Rays* Z54.1. 54 pp. New York: American Standards Association, 1946.
2. New York City Department of Health. *Sanitary Code.* Section 107a effective March 1, 1948.
3. *Requirements for the Safe Operation of Fluoroscopic Shoe Fitting Devices.* 5 pp. Bureau of Industrial Hygiene, Detroit Department of Health, Detroit, Michigan, December, 1948.

POTENTIAL DANGERS IN THE UNCONTROLLED USE OF SHOE-FITTING FLUOROSCOPES*

L. H. Hempelmann, M.D.†

BOSTON

THREE types of radiation injuries may result from the uncontrolled use of low-voltage x-ray machines in shoe stores in the manner described by Dr. Williams in the preceding article. The most likely injuries are interference with normal foot development of children who are fluoroscoped repeatedly when being fitted with new shoes; acute radiation burns of the customer's feet resulting in late permanent skin damage; chronic radiation injury of the blood-forming tissue of store employees who work with improperly shielded x-ray machines. Little is known concerning possible effects of this type of radiation on the sex glands. Some of the unusual features of these injuries will be discussed, and the possibility of their being caused by existing shoe-fitting fluoroscopes will be considered.

Possible Types of Injury

Interference with Foot Development

Growing bone, in contrast to adult bone and hyaline cartilage, is easily damaged by exposure to x-rays. This is due to the radiosensitivity of the epiphyseal cartilage. Damage to this tissue is manifested by reduction in the rate of bone growth and by premature closure of the epiphyseal junction. Experimental studies in animals of the action of x-rays on the epiphyses bring out certain facts that are related to the present problem. It has been shown that the younger the animal, the greater the effect on bone growth of a given dose of x-rays.[1] In addition, stunting of bone growth in animals can be produced by less than half the dose of 200 kv that will cause erythema of the overlying skin. It has also been demonstrated that fractionation of the dose and prolongation of the intervals between exposure lessen the effect of the radiation on epiphyseal cartilage, as well as on other tissue.[2]

Clinical reports describe cases of cessation of bone development in children who receive radiation therapy for lesions in the region of the epiphyses.[2] Therapeutic use has been made of the growth-stunting property of x-rays to minimize inequality in limb length caused by osteomyelitis or other types of bone disease.[3] The minimal stunting dose of x-rays has been stated to be a quarter of the erythema dose for infants and half the erythema dose in older children.[4] If this statement is correct, a few hundred of moderately hard x-rays administered in a single exposure will cause a disturbance in foot development in young children.

Aside from the fact that the epiphyses are extremely radiosensitive, the most important lesson to be learned from clinical experience and from animal experimentation is that abnormal bone development can be produced insidiously in the absence of skin damage or other external evidence of radiation injury. Before the other types of radiation damage are considered, it should be stated

*From the Medical Laboratories, Collis P. Huntington Memorial Hospital.
This is publication No. 672 of the Harvard Cancer Commission.
†Special assistant to the director of the Division of Biology and Medicine, United States Atomic Energy Commission; consultant in biophysics, Massachusetts General Hospital; research associate, Harvard Medical School.

that the dosages mentioned in the literature usually refer to more penetrating radiation than that delivered by shoe-fitting fluoroscopes. Consequently, the dose of soft x-rays necessary to damage epiphyseal tissue lying 1 or 2 cm. below the skin surface would be more nearly equal to the erythema dose.

Radiation Burns of the Skin

The acute and chronic types of x-ray reactions of the skin are so well known that they need not be described. Innumerable cases of such injuries have been reported in the last fifty years, and yet the data concerning the radiation dosages that cause skin damage, except for that delivered as an acute exposure, are almost nonexistent. At least 600 to 1000 r of soft x-rays given within a day or two would be required to produce a serious skin reaction. If the radiation dosage were fractionated, higher total doses would be necessary to produce comparable skin damage. Little is known of the radiation dosages that cause chronic skin damage. It has been suggested that repeated exposure of the hands to 4 r of gamma rays per week over a period of many years may produce injury.[5] There is no published information bearing on the maximum radiation dosage that can be administered to the skin with safety at the intervals at which children are likely to be fitted for new shoes (two to four months).

Chronic Radiation Damage of the Blood-Forming Tissues of Store Employees

The hazards involved in repeated exposure of the body to soft x-rays are similar to those encountered in any hospital or physics laboratory that uses x-ray machines or radioactive material. The dangers to blood-forming tissues of chronic overexposure of the body to x-rays are familiar to everyone. Recent experiments illustrate how irradiation with small daily doses of x-rays reduces the life span of animals.[6] The maximum permissible dose of radiation to which persons can be safely exposed throughout their working lives has been considered for many years to be 0.1 r per day. Within the past few months, however, the Advisory Committee on X-Rays and Radium[7] has reconsidered this dose and recommended that it be lowered to 0.3 r per week.

Discussion

Consideration of the radiation dosages measured by Dr. Williams, in the light of the biologic information presented, suggests that injury to either the epiphyseal cartilage or the skin is unlikely after a single exposure to the shoe-fitting fluoroscope except under the most undesirable conditions. Several fittings within a day or two may conceivably lead to epiphyseal damage in children or to skin damage in children or adults. Repeated fluoroscopy of the foot by improperly regulated machines from early childhood to the age of normal closure of the epiphyses (eighteen to twenty years) could result in foot deformities and even in permanent skin damage.

To prevent injury to customers and employees, it is obvious that the use of x-ray machines in shoe stores must be controlled. Proper shielding of the fluoroscope to minimize radiation leakage, education of the users and store officials about the dangers involved in misuse of the machines and reduction of the foot dosage per viewing must be accomplished. Shielding of a low-voltage fluoroscope is a relatively simple matter. Conspicuous warning signs on each machine can help to educate the public to the dangers of too frequent use of fluoroscopy; restriction of the use of x-ray machines to qualified personnel will reduce the possibility of accidental overexposure. Reduction of the foot dosage per exposure can be accomplished by lowering of the tube output, by adequate filtration and by limitation of the exposure by automatic timing devices. Since the maximum amount of radiation that the foot can tolerate at intervals of several months is not known, it seems advisable to reduce the foot dosage to the minimum that is compatible with satisfactory use of the fluoroscope. As Dr. Williams has indicated, the foot can be visualized adequately in a fluoroscope that delivers 1 r in a five-second exposure. Therefore, the newly issued recommendations of the Massachusetts Department of Hygiene (1 r per viewing, three exposures per day and twelve exposures per year) seem to be preferable to the higher dosages permitted by the American Standards Association and the New York City Health Department regulations quoted in the preceding article.

Summary

It may be said that the type of radiation injury most likely to result from the unsupervised use of low-voltage fluoroscopes in shoe stores is the malformation of the feet of growing children. Such deformities may occur in the absence of x-ray reactions of the skin. Skin damage of the feet of customers and injury of the blood-forming tissues of store employees are possible consequences of the misuses of the shoe-fitting fluoroscopes. These dangers can be controlled by proper regulation of the use of the machines.

References

1. Hinckel, C. L. Effect of roentgen rays on growing bones of albino rats. I. Quantitative studies of growth limitation following irradiation. *Am. J. Roentgenol.* **47**:439-457, 1942.
2. Bisgard, J. D., and Hunt, H. B. Influence of roentgen rays and radium on epiphyseal growth of long bones. *Radiology* **25**:56-64, 1936.
3. Spangler, D. Effect of x-ray therapy for closure of epiphyses: preliminary report. *Radiology* **37**:310-315, 1941.
4. Flaskamp, W. Über Röntgenschäden und Schäden durch radioaktive Substanzen. *Sonderbande zur Strahlen. Therap.* **12**:136-143, 1930.
5. Parker, H. M. Private communication to R. S. Stone. Cited by Parker, H. M. Health-physics, instrumentation, and radium protection. *Adv. Biol. & M. Physics* **1**:223-285, 1948.
6. Lorenz, E., Heston, W. E., Eschenbrenner, A. B., and Deringer, M. K. Biological studies in tolerance range. *Radiology* **49**:274-285, 1947.
7. *Medical X-ray Protection up to Two Million Volts.* Handbook 41. U. S. Department of Commerce, National Bureau of Standards, March 30, 1949.

MEDICAL PROGRESS

GASTROINTESTINAL ALLERGY (Concluded)*

FRANZ J. INGELFINGER, M.D.,† FRANCIS C. LOWELL, M.D.,† AND WILLIAM FRANKLIN, M.D.‡

BOSTON

LABORATORY TESTS

In patients suspected of gastrointestinal allergy, demonstration of the allergic response has at times been sought by radiologic studies. For the most part, the patient has first been examined by means of a barium-in-water meal, followed in a few days by a similar examination, a suspected food being given with or a few hours after the barium suspension. In patients so examined, whether adults or children, the most common finding at the second test was delayed gastric emptying, usually interpreted as indicating allergic pyloric spasm or edema.[31, 40, 63, 64] This interpretation, however, may be questioned on many counts. All foods, particularly those containing fats, may delay gastric evacuation. In normal children, the painstaking studies of Macy et al.[65, 66] show that a barium-water meal leaves the stomach in one and eight-tenths to two and eight-tenths (average one and nine-tenths) hours, but that a barium-milk suspension requires one and five-tenths to four and five-tenths (average three and one-tenth) hours to leave the stomach. An adult stomach may evacuate all of a water meal within an hour but only 20 per cent of a milk meal of similar size.[67]

Against this background, the effects of an allegedly allergenic food cannot be differentiated easily from the normal effect of food on gastric emptying. In fact, those who appreciate that foods delay gastric evacuation postulate abnormal mechanisms only if this expected response does not occur. Thus, Macy et al.[65] observed that the milk meal emptied more rapidly than the water meal in one case. To explain this phenomenon, they invoked allergy. The same authors,[66] however, caution that "many factors are interrelated in the determination of the response of the alimentary canal: the method of measurement; the size of the meal ingested; its temperature, consistency, and content; the nutritional state of the individual; and the emotional and environmental condition to which the individual is subject at the time."

If gastric evacuation is delayed, the interpretation of pylorospasm is made, as pointed out by Fries and Mogil,[63] only by inference. Gastric evacuation is controlled by a number of factors. Of primary importance is gastric and duodenal motility rather than isolated spasm of the pyloric sphincter.[68] Hence, to explain retarded emptying of the stomach on this basis is usually incorrect.

The ingestion of an allergen is also credited with changing small-intestinal motility as demonstrated by a barium meal. The changes seen are irregular transport, abnormal luminal caliber and enlarged mucosal folds, the entire picture frequently resembling the so-called "deficiency pattern."[69] This pattern, however is not at all specific,[70] and adequate control studies are not available to exclude the likelihood that the observed changes were caused by food given irrespective of the presence of allergy. The ingestion of milk certainly may produce definite changes, either relaxation of intestinal loops or hypertonic segmentation, spasm and rapid transport. Whether this so-called "milk-reaction" is allergic in nature is discussed by Golden.[69] Although he states that "a diagnosis of intestinal allergy cannot be made on the basis of the roentgen examination at the present time," he believes that hypertonicity and rapid transit in the lower small bowel after the ingestion of milk or other foods suggests allergy. To support this contention, he presents a number of carefully documented cases, which, if allergic, again illustrate the inconstant characteristics of gastrointestinal allergy. In one case, allergy of the small bowel is demonstrable by a barium-in-water meal; in another, the meal must contain the offending food; in a third the ingestion of one egg is without effect, but a second induces disorder of motor function.

The difficulties of studying allergic reactions of the small intestine are shown in the objective and carefully evaluated work of Wing and Smith.[71] Of 9 patients studied after exposure to a supposedly allergenic food, 7 showed some variation in small-bowel pattern, but in only 3 was the change sufficient to exclude, in the authors' opinion, a non-specific reaction, and 1 of these suffered from mild ulcerative colitis. The same authors observed no change in the intestinal pattern of sensitized guinea pigs when the antigen was fed. Intravenous injection of the antigen produced anaphylaxis but no significant effect on the radiologic appearance of the small intestine.

X-ray study of the colon exposed to allergens has been fragmentary. In 17 patients given allergen-containing barium enemas, Fries and Mogil[63] de-

*From the Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.

†Associate professor of medicine, Boston University School of Medicine.

‡Assistant in medicine, Boston University School of Medicine.

tected signs of irritability, such as spasms and local constrictions.

In summary, radiologic study of the gastrointestinal tract occasionally reveals such marked derangements of appearance and motility after the ingestion of a food that a causal relation between the food and the observed reaction may be assumed, particularly if the x-ray findings are associated with symptoms. The problem is this: How can one be sure that the changes induced are allergic rather than nonspecific? A solution lies in more extensive use of control studies, adequate to exclude nonspecific effects. X-ray evidences of primary intestinal dysfunction are, as Weber[72] states, "presumably valid when properly controlled. In no field of roentgenologic diagnosis is the exercise of critical judgment and objectivity more necessary, if unwarranted deductions and correlations are to be avoided," and, in referring to the barium enema, "In my opinion the evidence of abnormal physiologic change brought to light with its use is highly unreliable. I hesitate to attach abnormal physiologic significance, for example, to a contracted portion of the sigmoid colon, to a general increase or decrease in the caliber and length of the intestine."

Direct observation of the gastric mucosa by means of the gastroscope should reveal whether this tissue displays transient urticarial edema as may the mucous membranes of the naso-oropharynx. A number of case reports illustrating precisely such a reaction have been collected from the European literature by Schindler.[73] Typical is the case of Chevallier,[74] that of a bee-keeper who, when stung by a bee, fainted, developed generalized urticaria and exhibited symptoms suggesting pyloric obstruction. Gastroscopy performed during one of these episodes revealed transient edema of the antral mucosa. Although the number of such cases is not large and the patients apparently were not seen by Schindler himself, he accepts acute allergic urticaria of the stomach as a rare but definite entity. In this, he receives strong support from the excellent studies of Pollard and Stuart.[75] These workers used the gastroscope to examine 6 patients before and after ingestion of foods that seemed to produce upper gastrointestinal symptoms. In each case ingestion of the food was followed in thirty to sixty minutes by symptoms, accompanied by changes involving the lower third of the stomach: hyperemia, broadening of the rugal folds, boggy edema, diminution of peristalsis and a lumpy appearance of the mucosa. Seven patients (some with asthma but no gastrointestinal symptoms) were studied as controls. The ingestion of foods in these cases also produced mucosal hyperemia and edema but, in the opinion of the authors, to a much less degree than in the patients with symptoms. Gastroscopic observations tend to strengthen the impression that allergic reactions may occur in the stomach.

Skin tests enjoy a varied reputation in the diagnosis of gastrointestinal allergy. The preparation of food extracts for skin testing is complicated by the tendency of certain substances to lose their allergenic activity very rapidly,[23] as well as by the occasional presence in foods of irritants that may produce skin reactions on some basis other than an allergic one. To these difficulties may be added the possibility[23, 11] that the allergen in some foods is a product of digestion, and special procedures may then be required for the preparation of suitable extracts.

Most workers have been discouraged with attempts to apply skin tests to the diagnosis of gastrointestinal allergy. Positive skin reactions, though generally regarded as indicating allergic sensitivity of the skin to the substance injected, do not necessarily indicate similar sensitivity of the gastrointestinal tract, nor are negative reactions considered adequate evidence on which to exclude it. These views are based on the absence of correlation between the reaction observed in the skin and the occurrence of gastrointestinal symptoms on exposure of the patient to the substance from which the extract was made.

In attempting to assess the significance of skin reactions in gastrointestinal allergy, we are faced with a further difficulty, which appears to us, for the present at least, to be unsurmountable. As pointed out in this review, the criteria on which a diagnosis of gastrointestinal allergy is usually based leave a good deal to be desired. It is clearly impossible to arrive at a conclusion regarding the value of skin tests in the diagnosis of gastrointestinal allergy until this entity has become better defined.

Variations in the number of leukocytes, eosinophils or thrombocytes following the ingestion of foods have been presented as criteria for making the diagnosis of gastrointestinal allergy.[29, 58, 64, 76-82] The best known of these tests is the leukopenic index, which was introduced in 1934 by Vaughan[76] as a means of detecting specific allergens that he believed were responsible for a variety of complaints, such as abdominal pain, urticaria, headache, neuritis, vertigo, asthma, colitis, eczema and indigestion. The usual manner of carrying out this test is as follows: two specimens for white-cell counts are drawn at ten-minute intervals in the fasting state; the test food is then eaten, and counts are done every fifteen minutes for an hour, and a final count is made at an hour and a half. A drop of 1000 cells per cubic millimeter below the mean of the two fasting counts is considered to signify hypersensitivity to the food ingested. The validity of this test is disputed,[84, 85] and its technic is open to criticism. Loveless et al.[84] showed that leukocytosis is not the normal response to the ingestion of foods, thus invalidating one of the premises upon which this test is based. Furthermore, postprandial leukopenia occurred with equal rarity

in both food-sensitive and nonsensitive subjects, and the incidence of this leukopenia was that which might result from the random variations that occur in the performance of successive blood counts. Loveless[84] also demonstrated that the development of asthma, hay fever and urticaria in a small group of ragweed-sensitive patients given ragweed extract subcutaneously was not associated with significant change in the leukocyte level. These findings were confirmed by Brown and Wadsworth,[85] who found no proof of the existence of either postprandial leukocytosis or an anaphylactic postprandial leukopenia. In spite of this evidence, this test continues to be employed as a means of diagnosing food allergy.[77, 82] For this reason, it may be emphasized that in the usual technic of counting white cells, the error in duplicate samples may be as much as 20 per cent, and that the coefficient of variation is 10.7 per cent when the total count approximates 7000.[86] Consequently, the criterion of a reduction of 1000 cells per cubic millimeter that is used in the leukopenic index[76] would be met in about 1 out of 5 determinations on the basis of random variation alone. Spontaneous fluctuations in the number of circulating leukocytes further impair the significance of a 1000-cell change in the white-cell count.

Similar considerations apply to tests using a rise in eosinophils[78] or a fall in platelets[58, 82] as criteria for the diagnosis of an allergic gastrointestinal reaction to foods. Technical difficulties pertain particularly to the enumeration of thrombocytes. The technic of making eosinophil counts is usually not described in the papers employing this method. Hansen,[87] using a direct counting technic,[88] believed that a rise of 50 eosinophils per cubic millimeter after the ingestion of a food indicated hypersensitivity. As recent studies have amply demonstrated, however, the number of circulating eosinophils and white cells may be influenced by factors that are unrelated to allergy.[89]

Since Walzer[90] and Hecht et al.[91] suggest, on the basis of their experimental studies, that gastric acidity inhibits the gastrointestinal reaction to allergenic foods, the question arises whether patients with hypoacidity or anacidity are particularly susceptible to gastrointestinal food allergy. Individual case reports of patients believed to be suffering from such allergy mention gastric hypoacidity as a contributory factor,[21] but abnormalities of gastric secretion have not been observed when groups of patients suspected of having food or other allergies have been studied.[92-94]

The presence of eosinophils in fecal mucus has been adduced as evidence favoring the allergic nature of certain diarrheal disorders,[95] particularly ulcerative colitis.[6] Bockus,[42] on the other hand, writes, "cytologic examination of the stomach, bowel and rectal secretions has given little assistance in determining the etiologic basis of suspected gastro-intestinal allergy." Before the significance of eosinophils in rectal discharges or mucus can be evaluated, further cytologic procedures, such as Bercovitz's[96] examination of rectal material in various intestinal disorders, appear necessary. Although eosinophilia is frequently associated with the body's reaction to foreign or altered protein, reactions of this type may be the result as well as the cause of a disease. Thus, a necrotic neoplasm may provoke eosinophilia,[97] and in a similar fashion, eosinophilia in a disease like ulcerative colitis may merely be the result of tissue destruction. If this is true, interpretation of eosinophils in rectal discharges is difficult.

Summary

The experimental production in animals and man of reactions in the gastrointestinal tract due to contact of sensitized tissue with antigen (allergen) appears to be established. Evidence for the spontaneous occurrence of gastrointestinal allergy in man is good but not conclusive. The incidence of such reactions, assuming that they occur, cannot be determined at the present time for a number of reasons: the symptoms of so-called gastrointestinal allergy are common to many conditions and are prevalent in a considerable portion of the population; there are apparently no manifestations peculiar to gastrointestinal allergy alone; and the methods commonly used for diagnosis are not sufficiently accurate. The validity, in particular, of indirect tests, such as skin tests, changes in the number of blood cells or x-ray findings unaccompanied by symptoms cannot be assessed at present. These tests are reliable only to the extent that results can be correlated with proved gastrointestinal allergy, cases of which appear to be exceedingly rare.

Proof that a patient's gastrointestinal symptoms are on an allergic basis theoretically could be achieved if the following requirements were fulfilled: the symptoms should be caused by contact with a specific substance that is innocuous to the bulk of the population, an immune mechanism should be evident in their pathogenesis, and lesions or functional changes in the gut should be demonstrable. These requirements are difficult if not impossible to meet with present knowledge or technics. However, it seems reasonable to make the diagnosis of gastrointestinal allergy if gastrointestinal symptoms invariably follow contact with a normally inactive substance, and if other causes such as psychic effects and mechanical irritation are excluded. Regarding foods, the following criteria are suggested: the food should be given in capsules by stomach tube or in such a manner that the patient is unaware of its nature; reproducible symptoms, signs or x-ray findings should consistently follow administration of the disguised food at a more or less constant interval, possibly not to exceed a

few hours; other foods given to the patient in the same manner should not produce similar changes; and the suspected food given in the same manner to normal subjects should not cause the observed effects.

The fulfillment of these criteria for the diagnosis of gastrointestinal allergy would be a laborious procedure. If the diagnosis could be firmly established in a number of cases, a characteristic clinical pattern might become apparent and correlation with indirect tests might be possible.

References

63. Fries, J. H., and Mogil, M. Roentgen observations on children with gastrointestinal allergy to foods. *J. Allergy* **14**:310-321, 1943.
64. Randolph, T. G., and Rowling, E. F. A. Blood studies in allergy: cellular reactions in sulfonamide sensitivity. *J. Allergy* **16**:17-29, 1945.
65. Macy, I. G., Reynolds, L., Souders, H. J., and Olson, M. B. Normal variation in gastrointestinal response of healthy children. *Am. J. Roentgenol.* **43**:394-403, 1940.
66. Reynolds, L., Macy, I. G., Hunscher, H., and Olson, M. B. Gastrointestinal response of average, healthy children to test meals of barium in milk, cream, meat and carbohydrate media. *Am. J. Roentgenol.* **43**:517-532, 1940.
67. Gershon-Cohen, J., and Shay, H. Experimental studies on gastric physiology in man. III. Study of pyloric control. Rôle of milk and cream in normal and in subjects with quiescent duodenal ulcer. *Am. J. Roentgenol.* **38**:427-446, 1937.
68. Quigley, J. P. Modern explanation of gastric emptying mechanism. *Am. J. Digest. Dis.* **10**:418-421, 1943.
69. Golden, R. *Radiologic Examination of the Small Intestine.* 239 pp. Philadelphia: J. B. Lippincott Co., 1945.
70. Ingelfinger, F. J. Clinical significance of changes in small intestinal function. *Connecticut M. J.* **12**:106, 1948.
71. Wing, W. M., and Smith, C. A. Spontaneous and induced sensitivity to foodstuffs: x-ray studies of small intestine in man and guinea pig. *J. Allergy* **14**:56-64, 1942.
72. Weber, H. M. Roentgenologic contribution to diagnosis of functional intestinal disorders. *J. A. M. A.* **134**:226-229, 1947.
73. Schindler, R. *Gastritis.* 462 pp. New York: Grune & Stratton, 1947.
74. Chevallier, R. Cited by Schindler.[73]
75. Pollard, H. M., and Stuart, G. J. Experimental reproduction of gastric allergy in human beings with controlled observations on mucosa. *J. Allergy* **13**:467-473, 1942.
76. Vaughan, W. T. Food allergens. III. Leucopenic index: preliminary report. *J. Allergy* **5**:601-605, 1934.
77. Squier, T. L. Leucocyte fragility in transitory leucopenia. *J. Allergy* **17**:197-202, 1946.
78. Squier, T. L., and Madison, F. W. Hematologic response in food allergy eosinophilia in leucopenic index. *J. Allergy* **8**:250-256, 1937.
79. Vaughan, W. T. Further studies on leucopenic index in food allergy. *J. Allergy* **6**:78-85, 1934.
80. *Idem.* Food idiosyncracy as factor in digestive leucocyte response. *J. Allergy* **6**:421-430, 1935.
81. Rinkel, H. J. Leucopenic index in allergic diseases. *J. Allergy* **7**:356-363, 1935.
82. Hanson, J. F. Effects of food combinations upon leukopenic index determinations, and upon body temperature. *Am. J. M. Sc.* **201**:11-30, 1941.
83. Pohle, F. J., and Cohen E. B. Variations in blood platelets in allergic individuals following ingestion of test foods. *J. Lab. & Clin. Med.* **32**:1395, 1947.
84. Loveless, M., Dorfman, R., and Downing, L. Statistical evaluation of leucopenic index in allergy. *J. Allergy* **9**:321-344, 1938.
85. Brown, E. M., and Wadsworth, G. P. Leucopenic index. *J. Allergy* **9**:345-370, 1938.
86. Berkson, J., Magath, T. B., and Hurn, M. Error of estimate of blood cell count as made with hemocytometer. *Am. J. Physiol.* **128**:309-323, 1940.
87. Hansen, K. Gastritis allergica. *Deutsche med. Wchnschr.* **67**:197-203, 1941.
88. Dunger, R. Eine einfache Methode der Zählung der eosinophilen Leukozyten und der praktische Wert dieser Untersuchung. *Munchen. med. Wchnschr.* **57**:1942-1944, 1910.
89. Forsham, P. H., Thorn, G. W., Prunty, F. T., and Hills, A. G. Clinical studies with pituitary adrenocorticotropin. *J. Clin. Endocrinol.* **8**:15-66, 1948.
90. Walzer, M. Allergy of abdominal organs. *J. Lab. & Clin. Med.* **26**:1867-1877, 1941.
91. Hecht, R., Mosko, M. M., Lubin, J., Sulzberger, M. B., and Baer, R. L. Absorption of whole ragweed pollen from gastrointestinal tract. *J. Allergy* **15**:9-13, 1944.
92. Vanzant, F. R., Alvarez, W. C., Berkson, J., and Eusterman, G. B. Changes in gastric acidity in peptic ulcer, cholecystitis and other diseases. *Arch. Int. Med.* **52**:616-631, 1933.
93. Loveless, M. Gastric acidity and acid therapy in allergy. *J. Allergy* **7**:203-223, 1936.
94. Phillips, K. Studies on neutralization test of gastric acidity in relation to general disease. *Am. J. Digest. Dis.* **4**:87-91, 1937.
95. Nance, F. D. Stool eosinophilia in gastrointestinal allergy of infancy. *J. Pediat.* **33**:313-317, 1948.
96. Bercovitz, Z. Studies in cellular exudates of bowel discharges. III. Diagnostic significance of cellular exudative studies in chronic bowel disorders. *Ann. Int. Med.* **14**:1323-1340, 1941.
97. Wintrobe, M. M. *Clinical Hematology.* Second edition. 862 pp. Philadelphia: Lea & Febiger, 1946.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 35351

PRESENTATION OF CASE

A thirteen-year-old boy was admitted to the hospital with the chief complaint of pain in the back and right leg.

Six months before admission the patient fell on the ice and struck his sacrum. For about a week he felt considerable pain, but then was asymptomatic for two months. Four months before entry he noted the sudden onset of a steady, dull pain in his right groin, associated with a temperature up to 102°F. He was admitted to a community hospital, where an appendectomy was performed. Apparently the appendix was normal. Almost immediately after discharge he complained of right lumbosacral backache, general malaise and nausea. The temperature rose to 102°F., and he was readmitted to the hospital. The back pain radiated to the left, and he also complained of pain in and behind the right knee. Since then the pain had been more or less constant and was aggravated by movement and palpation. During this four-month period he noted weakness of the legs. He also had anorexia, weight loss, several episodes of epistaxes and easy bruising of the lips. He had recurrent fever, with true chills, and frequent episodes of delirium. The past history was noncontributory.

Physical examination revealed a pale, emaciated boy complaining of pain in the right knee and back. There was no peripheral lymphadenopathy except for small, shotty inguinal lymph nodes. The lungs were clear. There was a Grade II systolic murmur along the left sternal border. Examination of the abdomen disclosed tenderness in the left upper quadrant, but no definite mass was felt. The liver edge was just palpable, and the spleen was not felt. A fleeting, spherical, firm mass was palpable above the left inguinal ligament. Examination of the extremities revealed marked wasting of the legs and atrophy of both quadriceps.

There was tenderness along the sciatic nerve from the great sciatic notch to the calf, and to the right of the third and fourth lumbar vertebras. The lumbar spine was fixed in slight flexion. The motion of the right hip was extremely painful. The patient walked with a slight limp on the right.

Neurologic examination revealed general weakness of the legs and arms and atrophy of both quadriceps. The deep reflexes were hypoactive. The plantar reflexes were down. Sensation was intact throughout. The eyes were normal except for slight blurring of the disks. There was no nystagmus — horizontal or vertical.

The blood pressure was 110 systolic, 80 diastolic. The temperature was 99°F., the pulse 100, and the respirations 22.

Urinalysis revealed no abnormality. The white-cell count ranged from 7700 to 4000, with a normal differential on admission changing to one in which 9 per cent of peculiar cells called "plasma cells" were found. The hemoglobin was 10.6 gm. on admission. There was hypochromia, anisocytosis, poikilocytosis and polychromasia.

A bone-marrow aspiration of the first lumbar vertebra revealed on one of several stained specimens a sheet of abnormal cells that appeared to resemble plasma cells or malignant tumor cells.

The stools were guaiac negative. The total protein was 7.6 gm. per 100 cc., with an albumin of 4.7 gm. and a globulin of 2.8 gm. The nonprotein nitrogen was 24 mg., the calcium 10.1 mg., the phosphorus 4.9 mg., and the alkaline phosphatase 6.1 units per 100 cc.

The cerebrospinal fluid was normal. An electromyogram showed an abnormal record: there were spontaneous fasciculations in the muscles of the upper extremities.

X-ray examination of the chest and abdomen was negative. X-ray examination of the bones revealed diffuse granularity of all the bones of the lumbar spine and pelvis, suggesting demineralization. An area of destruction was disclosed in the body of the fifth lumbar vertebra and another in the left tenth rib in the axillary line.

The patient ran a low febrile course, with significant progressive weight loss and frequent episodes of lower lumbar pain extending down to the right leg. On several occasions he experienced severe crampy pain radiating from the thoracic spine. The pain was sufficiently severe to require the administration of morphine on several occasions.

On the twenty-fourth hospital day a segment of the tenth left rib was removed.

DIFFERENTIAL DIAGNOSIS

DR. CHARLES S. KUBIK: I think it should be stated that not only were the knee jerks weak but also there was a marked difference between the right and the left. The right was considerably weaker than the left.

Dr. Ralph A. Ross: In summary, we have a thirteen-year-old boy with an injury to the lower back, who was asymptomatic after a period of a week. Two months later, he had pain in the region of the injury, extending down the right leg, associated with recurrent fever, chills, delirium, anorexia, anemia and a hemorrhagic tendency, with evidence of neurologic difficulty as brought out by Dr. Kubik.

Examination showed a basal systolic murmur in the heart, possibly due to the increasing anemia, and evidence of a lesion in the lower lumbar region, with probable involvement of the sciatic nerve on the right, a lesion in the left rib and a possibility of some intracranial or posterior orbital lesion to explain the blurring of the disks.

May we see the x-ray films?

Dr. Stanley M. Wyman: These films were taken on two different dates. In the first group the chest and heart appear within normal limits. There is definitely a destructive lesion in the left tenth rib as described in the protocol. It seems to be purely osteolytic, with no evidence of bone reaction. This particular film shows no evidence of expansion of the bone.

Dr. Walter Bauer: How about the ribs on the right?

Dr. Wyman: I think these are vascular markings that extend across the rib and create a pseudodefect. I do not believe it is a true lesion in the rib. However, a diffuse granularity is seen throughout all the bones of the lumbar spine, pelvis and upper femur. In the films taken a month later the fifth lumbar vertebra shows a diffuse denseness throughout its entire body, with a suggestion of some irregular destruction of the anterior portion and possibly the lower posterior angle of the body.

Dr. Ross: Are there any films of the upper extremities?

Dr. Wyman: There are none available.

Dr. Ross: The patient had a traumatic injury six months before hospital admission apparently not related to his subsequent illness. However, one might consider that it had initiated the train of events that led to the symptoms bringing him to the hospital. I do not believe that injury would explain the picture we are dealing with.

Could infection have been the main factor in this picture? The systemic symptoms, the malaise and the fever certainly could all be explained on the basis of general infection. He had progressive anemia. Could the bone lesions, the destructive lesions in the fifth lumbar vertebra and the tenth rib have been on the basis of localized infection? That does not, however, satisfy the description of the generalized granularity — the demineralization of the bones in the pelvis.

So far as neoplasms — localized neoplastic disease, such as Ewing's tumor or osteogenic sarcoma — are concerned, again, the fever, the systemic signs and the central-nervous-system signs would fit primary bone tumor with metastases. However, I think after a period of four months the x-ray diagnosis should have been more definite, and the normal serum phosphatase indicates a destructive lesion without new bone formation, which would be against the diagnosis of primary bone tumor. The widespread involvement of the bone marrow, as evidenced by the leukopenia, the progressive anemia and the hemorrhagic tendency, suggests a neoplasm, primarily involving the medullary tissue.

Hodgkin's disease comes up for consideration — a rare condition in the pediatric age group — in this case appearing largely in the medullary tissue. I do not believe it was Hodgkin's disease.

Multiple myeloma gives a picture of diffuse bone disease. A normal serum protein is against the diagnosis as is the fact that this is a very rare condition in childhood. Aleukemic leukemia would again explain the picture of the widespread medullary disease, the large lesions in the lumbar spine and rib. Vague masses in the abdomen could be explained on the basis of large areas of leukemic infiltration. The finding of "plasma cells" in the pleural fluid and the suggestion of similar cells seen in smears of bone-marrow aspiration make the possibility of a lymphatic leukemia of the plasma cell type a likely one. This disease, although it is rare, is sometimes seen in the pediatric age group as one of the chronic leukemias and may cause findings such as those described.

Another neoplastic disease that I should like to consider is neuroblastoma, the commonest of the bone diseases in children. It involves the retroperitoneal space, the orbits and the intracranial structures and is often evidenced mainly by involvement of the medullary tissue. Because of the statistical probability, I shall leave my diagnosis as neuroblastoma involving mainly the fifth lumbar vertebra and the tenth rib on the left side, with general spread to the medullary tissue.

DR. KUBIK: This clinical summary does not begin to indicate the difficulties encountered in making the diagnosis. There was a considerable difference of opinion among clinicians and radiologists regarding the significance of the x-ray findings, which now seem so clearly defined. The lesion in the rib was not discovered until after the patient had been in the hospital for some time. He looked very ill, he had lost weight, and nearly every movement resulted in pain, so that the question of generalized tumor involvement had to be most thoroughly investigated.

DR. BAUER: I wonder, since he had "plasma cells" in the smear, with similar cells having been found in the bone-marrow aspirations, why the surgeons chose to do a resection of the rib to be certain what they were dealing with. With that amount of evidence there must have been some question about the plasma cells, both in the smear and in the marrow.

DR. FRANK B. NORBURY: They were seen by several people, who were sure they were abnormal cells, and the term "plasma cell" was the most logical one for them. We thought that biopsy would give a more direct answer than aspiration alone.

DR. L. S. P. DAVIDSON (Edinburgh): I think the cytology of these cells is important. The patient was suffering from some diffuse malignant process involving many bones. I do not believe the absence of Bence-Jones bodies or changes in the plasma protein rule out multiple myeloma. Fifty per cent of the cases at the time of diagnosis do not have these changes. On the other hand, the findings of anemia, weakness, pain and temperature are frequently noted. It seems to me that because of the malignant process in the bone marrow, the cytology becomes of great importance. I do not believe one should rule out multiple myeloma because certain features are not present. If we accept the finding of "plasma cells," one should consider it seriously. The plasma-cell increase in the peripheral blood — 9 per cent — is interesting, and I have only seen 1 case — that was my first case, twenty-five years ago — in which multiple myeloma was associated with plasma cells in the peripheral blood. We have diagnosed 40 or 50 cases by radiology followed by sternal puncture or, frequently, by sternal puncture alone. I think this patient may well have had multiple myeloma.

DR. BENJAMIN CASTLEMAN: Have you seen it in a patient this young?

DR. DAVIDSON: I only see patients from fourteen years of age up, so I would not be able to answer that.

CLINICAL DIAGNOSIS

Neuroblastoma?
Multiple myeloma?

DR. ROSS'S DIAGNOSIS

Neuroblastoma.

ANATOMICAL DIAGNOSIS

Neuroblastoma, metastatic, of rib.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The rib biopsy demonstrated neuroblastoma — a classic one showing small cells with the characteristic grouping in so-called rosettes. It is interesting to recall that the neuroblastic origin of this tumor was first clearly proved in this building in 1910 by Dr. James Homer Wright,[1] then director of the laboratory, though the possibility of such an origin had been suggested by Marchand[2] as early as 1891. Until then they were called small-cell sarcoma or lymphoma, and it was Wright who described 5 cases and showed that the tumor cells produced nerve fibrils. Here are some of Dr. Wright's original lantern slides, showing the rosettes very clearly.

DR. ROSS: Would the finding in the bone marrow fit in with the picture one sees at autopsy?

DR. CASTLEMAN: I did not see the bone-marrow aspiration, but I think it is quite probable that neuroblasts may have been mistaken for plasma cells. Neuroblasts are pear-shaped cells, and the nucleus is characteristically eccentric.

REFERENCES

1. Wright, J. H. Neurocytoma or neuroblastoma, kind of tumor not generally recognized. *J. Exper. Med.* 12:556-561, 1910.
2. Marchand, F., Beitr. z. Kenntnis der Glandula Carotica und der Nebennieren. *Internat. Beitr. z. Wissensch. Med.* 1:578, 1891.

CASE 35352

PRESENTATION OF CASE

A forty-five-year-old housewife entered the hospital complaining of pain in the right lower quadrant.

Six months prior to admission the patient noticed a mass in the lower abdomen, which grew steadily and rapidly until admission. During this period she had three attacks of pain in the right lower quadrant, the first two preceding her menstrual periods. The pain was sharp, moderately severe and nonradiating.

The third attack occurred on the morning of the day of admission and was similar to the others but considerably more severe. There were no other symptoms. The last menstrual period began eight days before admission and lasted six days, the duration and flow being considered normal. Menses occurred every twenty-eight days and were usually preceded by a slight mucoid discharge. There had been no weight loss, change of bowel habits, menorrhagia or urinary symptoms.

The patient had been married thirteen years and had four children ranging in age from twelve to four years. She had had fairly severe rheumatoid arthritis for the past ten years.

Physical examination revealed a moderately tender mass in the lower abdomen, extending to the level of the umbilicus. It was about the size of a five-months' pregnant uterus, and was only slightly movable. The abdomen was stretched over the mass, and spasm could not be accurately evaluated. Peristalsis was normal. On pelvic examination the cervix was normal. The uterus could not be defined, but the cervix was not fixed. The mass was easily palpable but too large to enter the true pelvis. The vaults contained no other tumors. There was a slight, white, stringy vaginal discharge. The chest and heart were normal.

The temperature was 98.6°F., the pulse 66, and the respirations 16. The blood pressure was 158 systolic, 84 diastolic.

The hemoglobin was 85 per cent, and the white-cell count 18,800. The urine was normal. A barium enema showed the terminal ileum displaced into the right upper quadrant by a mass in the lower abdomen. The colon was normal. An intravenous pyelogram was interpreted as being normal, except for some evidence of pressure on the lower ends of both ureters by a large irregularly outlined, homogeneous mass extending from the pelvis upward. No tumor cells were found by vaginal smear. A rabbit test for pregnancy was negative.

On the third hospital day the temperature rose to 101°F., and the pulse to 100. The prothrombin time was 29 seconds (normal, 19 seconds). The respirations remained normal. The abdominal mass became progressively more tender on each succeeding day. In a chest film taken on the fourth day there was a small linear area of increased density above the right leaf of the diaphragm laterally. The prothrombin time rose to 41 seconds, and the white-cell count was 20,800. The temperature remained elevated between 100 and 103°F.

An operation was performed on the seventh hospital day.

Differential Diagnosis

Dr. Francis M. Ingersoll: In the discussion of this case there are three outstanding things that have to be correlated. First we note that the patient had an obvious tumor mass in the lower abdomen of six months' duration. We do not know what this mass was but will try to make a diagnosis. The second important point is that some change occurred in the mass that caused pain and precipitated hospital admission. The third point is that her hospital course was characterized by fever, leukocytosis and prostration. An elevated prothrombin time was discovered, which may be significant and may help to explain what happened within the mass. The hospital course suggests sepsis, and the possibility of sepsis in the tube, ovary or appendix must be considered and will be discussed later.

I would like to see the x-ray films to discover if they will give any leads in this situation.

Dr. James R. Lingley: It is interesting to note that the appendix is well visualized, so that the possibility of acute appendicitis or abscess is well ruled out. The mass extends out of the pelvis up to the level of the second lumbar vertebra, with pressure on the ureters. The ureters are filled down to the level of the mass. On the barium-enema examination the terminal ileum is displaced upward, outlining the upper border of the mass. It states in the protocol that the mass was irregular, but I would say that throughout most of the examination it is fairly smooth and not lobulated.

Dr. Ingersoll: The first problem is to try to decide what the mass was, or with which organ it was associated. The possibility that it was in the gastrointestinal tract is unlikely; the gynecologic system is much more probable. A tumor of the uterus of six months' duration would be either a sarcoma or a fibroid. Fibroids of this size rarely occur in women who have had four children, especially when the last pregnancy was only four years previous to the onset of symptoms, as it was in this particular case. The history of normal menses argues against a uterine tumor.

This tumor may have been a pathologic process associated with a fallopian tube. A tube filled with

blood might reach this size if it developed slowly. The elevated prothrombin time suggests that hemorrhage was possible, but such a condition is extremely unlikely. Pelvic inflammatory disease, with an abscess, could cause a tumor of this size, but this is also unlikely since if she had had pelvic inflammation for six months, she surely would have had other symptoms associated with this entity early in the illness. Something new or dramatic happened to this tumor just before this hospitalization, and tubal disease does not fit the picture.

Since we have eliminated the uterus and the tube, the tumor mass must have been in the ovary. When enlargements of the ovary are considered, endometriosis must be mentioned. This would have been an enormous endometrioma, but that is possible. Endometriosis, however, is unlikely in a para IV, since that disease — like fibroids — is usually seen in women who have two or less children. The mass could have been a dermoid cyst, pseudomucinous cyst, fibroma, ovarian cancer or any sort of ovarian tumor. Since we postulate that this mass was a tumor of the ovary, we now have to explain what happened to it to account for the symptoms that brought the patient to the hospital and made her so ill. There are three possible explanations: a twist of the cyst, with infarction; sepsis within a cyst, which occasionally occurs in the dermoid cyst; and hemorrhage into the cyst. The history does not state that the tumor increased markedly in size, but because of the elevated prothrombin time I think a sudden hemorrhage is the best explanation. I will narrow my diagnosis down to an ovarian tumor mass, possibly an endometrioma, with hemorrhage into it, to account for this clinical picture.

Dr. Benjamin Castleman: Dr. Klemperer, would you like to comment?

Dr. Friedrich W. Klemperer: I cannot see any relation of the rheumatoid arthritis to the mass. I wonder what medication the patient had. It is stated in the literature that salicylate medication, which patients with rheumatoid arthritis frequently receive, is sometimes associated with an elevated prothrombin time.

Dr. William Beckman: Our problem with this patient was somewhat different from Dr. Ingersoll's. She looked sick from the time of admission, and she did have severe chronic rheumatoid arthritis. While she was on the ward, she had a normal temperature for the first forty-eight hours and then began to develop this elevated temperature, which remained elevated. The problem, therefore, was to decide whether the fever was in any way related to the rheumatoid arthritis, which would have made surgery unwise. After a few days, having ruled out to the best of our knowledge any extra-abdominal cause for her fever, operation was performed. The preoperative diagnosis was infarction of a pedunculated fibroid.

Clinical Diagnosis

Infarcted pedunculated fibroid.

Dr. Ingersoll's Diagnosis

Hemorrhage into ovarian tumor, endometrioma?

Anatomical Diagnosis

Torsion and infarction of ovarian fibroma.

Pathological Discussion

Dr. Castleman: This patient was operated upon by Dr. Howard Ulfelder, who found a large right ovarian tumor that had twisted one and a half times on its pedicle. When received in the laboratory, the tumor measured 20 by 15 by 9 cm. and was deep red. The surface was covered with recently thrombosed tortuous veins, and the pedicle, which was 3 cm. in diameter, was also a collection of thrombosed vessels. On section the tumor was solid, soft and obviously infarcted. Microscopically it was a benign fibroma.

The New England Journal of Medicine

Formerly

The Boston Medical and Surgical Journal

Established 1828

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
and
THE NEW HAMPSHIRE MEDICAL SOCIETY

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND PUBLISHED WEEKLY UNDER THE JURISDICTION OF THE COMMITTEE ON PUBLICATIONS

Richard M. Smith, M.D., *Chairman*
James P. O'Hare, M.D. Conrad Wesselhoeft, M.D.
Oliver Cope, M.D. John Fallon, M.D.

Joseph Garland, M.D., Editor

ASSOCIATE EDITORS
Thomas H. Lanman, M.D. Donald Munro, M.D.
Henry Jackson, Jr., M.D.

Clara D. Davies, EXECUTIVE EDITOR
Robert O'Leary, ASSISTANT EDITOR

EDITORIAL BOARD
C. Guy Lane, M.D. Maxwell Finland, M.D.
Henry R. Viets, M.D. Carroll B. Larson, M.D.
Robert M. Green, M.D. C. Stuart Welch, M.D.
Dwight O'Hara, M.D. Vernon P. Williams, M.D.
Fletcher H. Colby, M.D. Benjamin Castleman, M.D.
Robert L. Goodale, M.D. Hugh R. Leavell, M.D.
Chester M. Jones, M.D. J. Englebert Dunphy, M.D.
Harvey R. Morrison, M.D. Charles H. Burnett, M.D.

SUBSCRIPTION TERMS: $7.00 per year in advance, postage paid, for the United States (medical students, $4.00 per year); Canada, $8.00 per year (Boston funds); $9.50 per year for all foreign countries belonging to the Postal Union.

MATERIAL should be received not later than noon on Thursday, three weeks before date of publication.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts. Telephone KE 6-2094.

A LOGICAL PROPOSAL

THE Committee on Membership of the Massachusetts Medical Society has approved and will recommend to the Council a change in Chapter V, Section 2 (b) of the by-laws. As at present worded the section reads:

> (b) The secretary of a district society shall receive an application from a graduate of a discontinued medical school, a foreign medical school or any medical school not approved by the Council only when:
>
> The applicant has possessed a license to practice medicine in the United States or its territories for at least five years.

The proposed change applies to the second paragraph, which would subsequently read:

> The applicant has possessed a license to practice medicine in the Commonwealth, and has conducted that practice in the district from which he makes application, for at least one year.

The reasons for such a change are apparent and seem logical. There are now no unapproved schools in existence in the United States, the period of great influx of graduates of foreign schools is over and, in fact, the recent graduates of most foreign schools are not now permitted even to take the examination for registration in Massachusetts. This condition will probably prevail at least until the Council on Medical Education and Hospitals of the American Medical Association has had made the investigation that it is sponsoring of foreign schools and issued its report.

Observation of a physician by his local colleagues for a year is of much greater value as a criterion than any number of probationary years elsewhere.

A five-year probationary period entails an unusual hardship on a physician who, because of lack of society membership, is debarred from staff privileges in many hospitals. It defeats the purpose of the Gallupe Plan, under which graduates of foreign or unaccepted schools are accorded supervised staff privileges. It defeats, indeed, the very purpose of medical organization, which is to ensure the delivery of the best medical care available to the greatest number of persons possible.

A COMMON RADIATION HAZARD

IN THIS era of rapid scientific and technologic advances and their practical applications to modern life, the physician has an added responsibility. More than ever he must be on his guard not only to diagnose the unforeseen pathologic patterns resulting from employment of new products and processes but also to protect the public if possible from their ill advised usage before untoward results occur.

The papers by Williams and Hempelmann published elsewhere in this issue of the *Journal* are examples of the type of diligence that must be observed in evaluating a newly commercialized device. From the careful data of Williams it is obvious that the use of such devices is not without danger. The variation of output and the protection provided among the apparatus tested varied widely. The amount of radiation received as direct

radiation by the customer and as scattered radiation by the salesforce represents a real potential hazard. Certainly, no warning plate bearing the inscription demanded by the American Standards Association Code can assure any degree of safety. Attention is called to the fact that unattended machines have been observed in use by children and young adults to study not only the bones of the feet but also those of the hands.

For the average busy adult there is less danger than for a child: he requires fewer fittings and has less time to satisfy his curiosity. The growing child, with several changes in footwear a year, presents the problem, as pointed out by Hempelmann, for he is the one who will be exposed to unknown amounts of radiation throughout his life, particularly during the growing period, and the late changes to the skin and particularly to his epiphyseal development must be anticipated and prevented.

The average fitting for a pair of shoes will require a minimum of two exposures, one for the child to observe, and a second for the parent. A few of the latest machines have duplicate viewing facilities for child and adult. These exposures will increase directly with the number of pairs of shoes tried on, the number of relatives or friends present and the innate curiosity of the child. It will be the exceptional salesperson who will risk loss of a sale by strict observance of any so-called safety code. There is also nothing to prevent the customer from shopping around in other stores boasting these modern marvels of shoe fitting.

Supposing a child is exposed to an erythema dose — and Williams's data show that on several machines this is reached with a few exposures — the delay of a week or two before skin changes manifest themselves allows them to be unnoticed or at best to be attributed to irritating socks or hot feet. If this insult is repeated many times permanent skin damages not only result but also the danger of epiphyseal damage and resulting foot deformities is encountered.

Blood changes and damage to the sex glands are less likely to occur as a result of customer exposure, but they become a definite possibility among the salesforce of the store. Knowledge of the safe daily amount of scattered radiation is far from complete. The maximum daily exposure thought to be safe has recently been scaled down from 0.1 r per day to 0.3 r per week as the result of studies made by the Advisory Committee on X-Rays and Radium.

The question raised by these papers is simply this: Are shoe-fitting fluoroscopes a necessity for the proper fitting of shoes or are they in effect sales promotional and of advertising value only— a form of window dressing? If the answer to the question is the latter they should be abandoned entirely. If the former answer is given, the strictest supervision is necessary, and unfortunately there is actually no safe method of making these restrictions work.

Fundamentally, the problem can be resolved only if machines, drugs and technics, particularly those giving off potentially dangerous radiation or having dangerous side reactions, are restricted in use to those whose training makes them competent to employ them.

THE CARE OF THE PATIENT

The statement of the Committee on Diabetes of the Massachusetts Medical Society elsewhere in this issue of the *Journal* deserves careful attention, not only because it points out that valuable information concerning the discovery and treatment of diabetes will soon be available but also because it demonstrates an attitude that epitomizes the best in medical practice. Regardless of the present furore over the future status of medicine in the United States, the primary concern of the doctor is unchanged: the welfare of the patient comes first. The program outlined has no relation to propaganda for or against state medicine, but the content of the message, which justifies the confidence of the patient in his physician, should be widely publicized.

In the midst of the present controversy, the proposed campaign is reassuring and edifying. The medical profession has not deviated from its ideal of service — the primary goal of ceaseless effort to find the best means of recognizing and curing disease. The tidings of what can be an immense forward step in the diagnosis and treatment of a

disease that is one of the major causes of death may well prove more effective than more emotional approaches to the public on the score of the future of medical practice: organized medicine, not resting on its laurels or even emphasizing previous discoveries and achievements, is committed to progressive endeavor in all branches of the science of healing.

Here, then, is information that may justifiably be incorporated in the educational program being conducted by the leaders of American medicine — to prove, to those who are ignorant of, or in doubt about, its aims, that to the medical profession the care of the patient comes first; if and how to regulate the service rendered are matters of secondary importance. The plan outlined, and others like it, may well affect the public's answer to the question of who is best fitted to control the practice of medicine.

SEA-GOING ARMY

To BE rocked in the cradle of the deep may yet become the pleasant experience suggested by the old song, according to the release earlier this year from the Department of the Army of the National Military Establishment. It may be that the sponsorship, by the Army Medical Department alone, of the now well known drug that acts as both a preventive and cure of seasickness implies a situation well in hand in the Navy; it may be that the boys in blue are simply willing to continue taking it on the chin and when the breezes blow to "generally go below."

Credit for the discovery of Dramamine, the salvation of those who go down to the sea in ships, belongs to Dr. Leslie N. Gay, of the Protein Clinic of Johns Hopkins University Hospital, and Dr. Paul Carliner, likewise a member of the Johns Hopkins staff. The United States Army Transport *Ballou*, loaded with more than 400 defenders of that which lies between the shining seas, provided the impressive clinical tests of the drug.

During an extremely rough passage in November, 1948, between New York and Bremerhaven, Germany, a total of 418 soldiers were treated with Dramamine. All were quartered in sub-level compartments. Complete relief from seasickness was obtained in 407 cases, with failure or only partial relief in 11. No unpleasant symptoms resulted from the drug itself.

Various control tests were made. In the preventive study one group was given Dramamine, and another group sugar capsules on the same schedule. Of the men receiving Dramamine, none developed nausea, and only 2 of the 134 became dizzy. Of 127 men who received the sugar capsules, 35 became seasick within twelve hours. All were relieved when placed on the Dramamine.

Of those who had remained well on Dramamine, 41 developed seasickness after the drug was omitted; 40 of these recovered spectacularly when it was again administered. Other men on the ship became ill, 195 of them severely. Of this group 187 were completely relieved within an hour after taking the first dose of Dramamine.

It appears that this boon to humanity, a chemical cousin of Benadryl and Pyribenzamine, has robbed the ocean of at least one of its perils.

Perhaps it should have become a top military secret.

—Mrs. Elizabeth Dodd died at St. Stephens, New Brunswick, a few weeks since, at the age of 111 years. She was born on board a British ship of war in the Bay of Biscay.— Ten days per annum is said to be the average sickness of human life.

Boston M. & S. J., *August 29, 1849*

MASSACHUSETTS MEDICAL SOCIETY

DIABETES DETECTION — A STATEMENT OF THE COMMITTEE ON DIABETES

THE existence of a large number of persons with diabetes undiagnosed and therefore untreated has been demonstrated by surveys not only in Massachusetts but elsewhere. There is need for the dissemination among physicians of information about the recent methods of treatment of diabetes by means of programs in district-society and hospital meetings. There is also a great opportunity and need to convey information to the public about the service the physician can give to patients with diabetes in all stages of the disease, but particularly

during the early stage. This affords an opportunity for carrying out the purpose of the National Education Campaign upon which the American Medical Association is now embarked. The purpose of this campaign is to demonstrate to the American people the services that physicians can render and are rendering to the American public in prevention of illness and the care of the sick.

The Committee on Diabetes of the Massachusetts Medical Society met in session on June 15, with representatives and presidents of fifteen of the district societies. They approved the program to be carried out in district societies aimed at disseminating information to the public by way of public meetings, the press and radio and at discovering patients with unrecognized diabetes so that they might come under medical treatment in doctors' offices and receive the benefits of modern treatment.

The Committee will have available an outlined plan for operation in any locality as well as printed material for distribution. A 16-mm., twenty-minute film in sound and color on diabetes for lay meetings has been prepared through the co-operation of the U. S. Public Health Service and the American Diabetes Association and will be available on loan through the office of the Massachusetts Department of Public Health. Strip films in color are also being prepared and will be available by loan to doctors for use in informing the public about diabetes and in treating patients.

New and simplified methods of self-testing, approved by the American Diabetes Association, will be available on sale at drug stores. These methods will make it possible for persons to make home tests of the urine following printed directions: these include advice to see the family physician for interpretation. Chemical materials for testing the urine will be provided by the manufacturers free of charge to any doctors' committee organized to carry out diabetes-detection programs, and approved by the district medical society, if application is made to the Massachusetts Committee on Diabetes, 8 The Fenway, Boston.

APPROVED BY VOTE

FRANK N. ALLAN
GEORGE BALLANTYNE
JOSEPH ROSENTHAL
JAMES TOWNSEND
PRISCILLA WHITE
HOWARD F. ROOT, *Chairman*

CORRESPONDENCE

FIRST PRINCIPLES

To the Editor: Dr. Alexander's article in the July 14 issue of the *Journal* certainly fills us all with horror. The editorial comment upon it is most appropriate. However, I wonder if we are sufficiently horrified. Do we not realize that the same ideology that Dr. Alexander describes has already been insidiously introduced to us and accepted by many of us?

Let us read again the article by Dean Sperry in the *Journal* of December 23, 1948, and the editorial pertaining to it. In that article euthanasia is discussed but not condemned. In fact, the woman who did away with her husband was considered fortunate because she suffered no remorse.

Let us get back to first principles. Most of us give lip service to God as the creator of life. Why then do we presume to usurp His authority over life, its beginning, its functions and its end? We seem to set ourselves up as gods to decide who should be born and when, who should be sterilized, who should have a lobotomy, who should be put out of his misery. If we believe in God why not leave such things to Him?

We seem to have lost the idea that the children and the aged, the insane and feebleminded, the sick and the weak offer us a means of working out our own eternal salvation. I am afraid that we look at them either as nuisances or as sources of revenue.

If a thing is good why not call it by its true name? It is only when we want to make an evil thing seem good that we invent a euphemistic name for it. Therefore, we have therapeutic sterilization, therapeutic abortion, planned parenthood and euthanasia.

If called by their true names — mutilation for the purpose of sterilization, murder of the unborn, prostitution of marriage and murder in the first degree — they would be instantly rejected as horrible. Are we so easily deceived by euphemistic terminology that we do not see that we are in danger of becoming fiends rather than physicians?

MARGARET C. MCMANAMY, M.D.

Orange, Massachusetts

STAIGE D. BLACKFORD

To the Editor: Dr. Staige Davis Blackford, of Charlottesville, Virginia, professor of the practice of medicine at the University of Virginia Department of Medicine and chief of gastroenterology at the University Hospital, died on July 17. He was well known in Boston and New England because of medical service at the Massachusetts General Hospital and because of his associations with many New England men during World War II as medical-service chief of the Eighth Evacuation Hospital in North Africa and Italy.

He came from an old and distinguished Virginia family of clergymen, physicians and educators. Among his forebears in the earliest history of the old Dominion were the thoughtful, liberal and moderate Southerners who opposed slavery in a practical way by freeing their Negroes and paying for their repatriation in Africa. When the Civil War arose, this liberal tradition did not prevent the family members then living from serving the Confederacy in many capacities.

Staige Blackford's life exemplified the family traditions of liberalism and of loyalty. His service to his country in both world wars, to his university and to his profession was as unremitting as it was selfless. His modesty, his forthright honesty, his always good-humored facility in exposing cant and pomposity, his disregard of personal ends brought public and academic recognition — some of us think, too little and too late. This irked his students and friends but not himself. His genius was friendship and sociability. He encouraged many colleagues, young and old, in their training and careers, in their research and in their medical writing. His intimates knew him best as a skillful but always amiable disputant and conversationalist who loved the night-long ceaseless argument. A host of friends and patients are witnesses that while he was among us he

"—— loved no darkness
Sophisticated no truth
Nursed no delusion
Allowed no fears."

ROBERT S. PALMER, M.D.

330 Dartmouth Street
Boston

BOOK REVIEWS

Index-Catalogue of the Library of the Surgeon General's Office. United States Army (Army Medical Library). Authors and subjects. Fourth series, Vol. X, M-Mez. 4°, cloth, 994 pp. Washington: United States Government Printing Office, 1948. $4.25.

The *Index Catalogue* was created by an Act of Congress in 1879 and began publication in 1880 and is now in the middle of the fourth series. The material in each series is arranged alphabetically by author and subject in one alphabet. The first series consisting of sixteen volumes, published from 1880 to 1895, was edited by Dr. John Shaw Billings, who brought the library to life after the Civil War and started it on its great career. The succeeding editions have been edited by Robert Fletcher, Fielding H. Garrison and Claudius F. Mayer, the present editor. In the first series Dr. Billings endeavored to present all the literature contained in the collections of the library, either in books and pamphlets or in periodicals and serials. The second series, of twenty-one volumes, covered the period 1896-1916, and the third series, of ten volumes, 1918 to 1932. The fourth series, now in process of publication, consisting of ten volumes, A-Me, 1936-1948, lists 7214 authors of books and pamphlets and 68,766 subject entries of material contained in books, pamphlets and periodicals. The subjects and their subdivisions total 6943. The last volume contains a check list of abbreviated titles of current publications received and indexed since 1919. Beginning at least with the third series, the indexing and publication of items became selective and did not represent the total number of titles of articles contained in the Library. The total number of volumes published to date is 57, covering a period of sixty-nine years. The total number of printed entries comprise 3,357,755, and the manuscript and printed catalogs of the Library total nearly 5,000,000 entries. The Army Medical Library is probably the largest and greatest medical library in the world. Its *Index Catalogue* provides for the world the greatest medical bibliography of all time. The great catalogs of the British Museum and the Bibliothèque nationale in Paris are devoted to the listing of all the manuscripts, books and pamphlets contained in these libraries. They do not list periodical and serial articles. In 1879 Dr. Billings began the publication of the *Index Medicus*, a current monthly periodical of medical literature. This continued through various trials and tribulations until 1927, when it consolidated with the rival list of the American Medical Association to form the present *Quarterly Cumulative Index Medicus*. At the present time the continuance of the catalog and the future of the *QCIM* are being considered by the top authorities in Washington and Chicago, and the fate of the catalog hangs in the balance. Much of the great reputation of the Army Medical Library is based on the *Index Catalogue*, and with its continuance or discontinuance this reputation will rise or fall as the case may be. Its discontinuance would constitute an overwhelming calamity, and the medical world would suffer a great loss. It is hoped that the decision will be favorable to its continuance.

On the Contributions of Hugh Owen Thomas of Liverpool, Sir Robert Jones of Liverpool and London, John Ridlon, M.D., of New York and Chicago to Modern Orthopedic Surgery. By H. Winnett Orr, M.D. With a supplement on *Ridlon and His Share in Moulding Orthopedic Surgery*, by Arthur Steindler. 8°, cloth, 253 pp. Springfield, Illinois: Charles C Thomas, 1949, $4.50.

In this volume Dr. Orr discusses the works and accomplishments of three great orthopedic surgeons, two British and one American. Preceding the text proper are biographies of Thomas, Jones and Ridlon. The text is divided into eight chapters including: a review of past and present methods in surgical practice (a review of past and present methods of surgical treatment, preface to several of Thomas's more important books); rest as a fundamental factor in the relief of pain and the arrest and cure of inflammation (introducing the famous Thomas splint); methods of obtaining rest in fractures and in articular disease; diagnosis and treatment of hip disease; disease of the knee joint, foot and ankle; the prevention and cure of disability and deformity in fractures; comments upon methods still in use in orthopedic practice, from the writings of H. O. Thomas, Sir Robert Jones and Dr. John Ridlon; and the influence of Hugh Owen Thomas, Dr. John Ridlon and Sir Robert Jones upon each other and upon orthopedic surgery. A supplement by Dr. Arthur Steindler discusses Dr. Ridlon and orthopedic surgery. An annotated bibliography concludes the text. The volume is well published, but the lack of an index and a table of contents detracts from its reference value. The book should be in all medical libraries and available to surgeons and orthopedists.

Fighting Spotted Fever in the Rockies. By Esther G. Price. 8°, cloth, 269 pp., with 165 illustrations and frontispiece. Helena, Montana: Naegele Printing Company, 1948. $4.00.

In this popular book the author relates the story of the struggle to control and prevent Rocky Mountain spotted fever in Montana. The campaign began in 1901, and was continuously hampered by professional jealousy, hostility by large real-estate interests, politics and nonco-operation of the population. In 1913 the State passed an act establishing a board of entomology that eventually obtained the co-operation of the federal authorities, leading to concentrated research and the identification of the virus of the disease and the discovery of the Spencer–Parker preventive vaccine. From the first makeshift woodshed laboratory to the modern Rocky Mountain Laboratory at Hamilton, Montana, has been a long and dangerous journey, a number of the staff succumbing to the disease. The laboratory today produces annually vaccine enough for 140,000 persons in the United States, Canada and Brazil.

The disease was originally found in the western states from the Canadian border to Nebraska and extending to the eastern portions of the Pacific Coast states. It has now spread to the Middle Atlantic states. Today, there are only six states in which the disease has not been reported: Maine, Vermont, Rhode Island, Connecticut, Michigan and Kansas. Three ticks have been proved transmitting agents of the virus of the disease: the Rocky Mountain wood tick, the American dog tick, and the rabbit tick, the three together having a wide distribution throughout the United States, Canada and Alaska. Because of existing conditions, it will not be possible to eradicate the ticks completely, but the vaccine provides effective protection for exposed persons.

An appendix gives the state laws of Montana of 1913 and 1919 affecting tick-control work in the Bitter Root Valley. The text concludes with a bibliography, and there are indexes of names and subjects. The story of this dramatic campaign is told in an interesting narrative style. The book should be in all medical libraries and in all medical-history collections.

NOTICES

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held in the classroom of the Nurses' Residence on Thursday, September 8 at 7:15 p.m. Cases will be presented and discussed by Drs. R. Adelaide Draper, Constance Curtiss and Clara Waldinger. Dr. Eliza A. Melkon will be chairman.

NEW ENGLAND SOCIETY OF ANESTHESIOLOGISTS

A regular meeting of The New England Society of Anesthesiologists will be held in the auditorium of Building A, Boston University School of Medicine, Boston, on Tuesday, September 13, at 8:00 p.m.

A round-table discussion entitled "Respiratory Problems in Acute Poliomyelitis" will be conducted by Drs. William Berenberg, Carlyle G. Flake, David Grice and Stanley Sarnoff. Dr. Robert M. Smith will be moderator.

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

Four sessions on research in medicine will be held in the Statler Hotel, New York, on December 28 and 29 as part of the 116th meeting of the American Association for the Advancement of Science.

These sessions are under the sponsorship of AAAS Section N, of which Dr. Gordon K. Moe, University of Michigan, is secretary.

(*Notices concluded on page xvii*)